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The SOCMA Sulfosuccinates Group (SSG) is pleased to submit its test plan and robust summaries as part of its voluntary effort in the HPV Challenge Program. There should be four attachments, all of which are .pdf files, accompanying this message. If all four are not attached, or if there is any difficulty in opening the attachments, please use the following contact:

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SSG Test Plan.pdf Dimethylbutyl Summaries.pdf Ethylhexyl Summaries.pdf Cyclohexyl Ester Summaries.pdf

AR201-13133A

TEST PLAN FOR SULFOSUCCINATES CATEGORY

June 13.2001

OVERVIEW

The SOCMA Sulfosuccinates Group (SSG) of the Synthetic Organic Chemical Manufacturers Association (SOCMA) hereby submits for review a test plan for a category consisting of three sulfosuccinates under the Environmental Protection Agency's {EPA) High Production Volume (HPV) Chemical Challenge Program. It is the intent of the panel and its member companies to use existing data on one or more of the sulfosuccinates to adequately fulfill the Screening Information Data Set (SIDS) for environmental fate endpoints, ecotoxicity tests, and human health effects for all three sulfosuccinates. The Sulfosuccinates Group believes that adequate data exist to fulfill all the requirements of the HPV program without the need for additional testing.

Test Plan Matrix for Sulfosuccinates

Chemical	Cyclohexyl (CAS # 23386-52-9)	Dimethylbutyl (CAS # 2373-38-8)	Ethylhexyl (CAS # 577-11-7)
PHYSICAL CHEMISTRY			
Melting point	E	E	E
Boiling point	NA	NA	NA
Vapor Pressure	NA	NA	NA
Water Solubility	Y	Y	Y
Kow	E	E	E
ENVIRONMENTAL FATE			
Photodegradation	E	E	E
Stability in Water	E	E	E
Biodegradation	Y	Y	Y
Transport between Environmental Compartments (Fugacity)	E	E	E
ECOTOXICITY			
Acute Toxicity to Fish	Y	Y	Y
Acute Toxicity to Aquatic Invertebrates	Y	C	Y
Toxicity to Aquatic Plants	Y	C	C
TOXICOLOGICAL DATA			
Acute Toxicity	Y	Y	Y
Repeated Dose Toxicity	Y	Y	Y
Genetic Toxicity-Mutation	Y	C	Y
Genetic Toxicity-Chromosomal Aberrations	C	C	Y
Carcinogenicity	C	C	Y
Toxicity to Reproduction	Y	Y	Y
Developmental Toxicity	C	C	Y
OTHER TOXICITY DATA			
Human Experience	NR	NR	Y
Pharmacokinetics	NR	NR	Y

Y = adequate experimental data ; NA = not applicable;
E = Endpoint fulfilled via EPIWIN model.
C = endpoint fulfilled by category approach; NR = not required

TABLE OF CONTENTS

1. Information about the Panel 3
2. Category Analysis 3
2.1 Identity of Category Members 3
2.2 Background Information on Category Members 3
2.3 Chemical Reactivity and Metabolism 5
3. Test Plan 5
3.1 Chemical and Physical Properties 5
3.1.1 Melting Point 6
3.1.2 Boiling Point 6
3.1.3 Vapor Pressure 6
3.1.4 Octanol/Water Partition Coefficients 6
3.1.5 Water Solubility 6
3.1.6 Test Plan for Physical Properties 7
3.2 Environmental Fate and Pathways.. 7
3.2.1 Photodegradation 7
3.2.2 Stability in Water 8
3.2.3 Biodegradation 8
3.2.4 Fugacity 8
3.2.5 Test Plan for Environmental Fate Parameters 9
3.3 Ecotoxicity 9
3.3.1 Acute Toxicity to Fish 9
3.3.2 Acute Toxicity to Aquatic Invertebrates.. 10
3.3.3 Acute Toxicity to Aquatic Plants.. 10
3.3.4 Acute Toxicity to Terrestrial Plants.. 10
3.3.5 Other 10
3.3.6 Test Plan for Ecotoxicity 10
3.4 Human Health Data.. 11
3.4.1 Acute Toxicity 12
3.4.2 Repeated Dose Toxicity.. 12
3.4.3 Genetic Toxicity.. 12
3.4.4 Carcinogenicity 13
3.4.5 Reproductive Toxicity 13
3.4.6 Developmental Toxicity.. 13
3.4.7 Human Experience 14
3.4.8 Test Plan for Mammalian Toxicity.. 14
3.5 Conclusion 14
4. References 16
5. Appendix 1 - Criteria for listing of robust summaries.. 20
6. Appendix 2 - Robust Summaries 20

1. Information about the Panel

The SOCMA Sulfosuccinates Group is formed under the sponsorship of the Association Management Center at the Synthetic Organic Chemical Manufacturers Association. The Panel consists of the following manufacturers or importers of sulfosuccinates:

Cytec Industries Inc.	MFG Chemical, Inc.
Finetex, Inc.	Rhodia Inc.
McIntyre Group, Ltd.	Uniquema

2. Category Analysis

2.1 Identity of Category Members

The substances included in the Sulfosuccinate Category are as follows:

Succinic acid, sulfo-, 1,4-bis(2-ethylhexyl) ester, sodium salt CAS No. 577-l 1-7
Designated as "Ethylhexyl ester."

Succinic acid, sulfo-, 1,4-bis(1,3-dimethylbutyl)ester, sodium salt CAS No. 2373-38-8
Designated as "Dimethylbutyl ester."

Succinic acid, sulfo-, 1,4-bis(dicyclohexyl)ester, sodium salt CAS No. 23386-52-9
Designated as "Cyclohexyl ester."

2.2 Background Information on Category Members

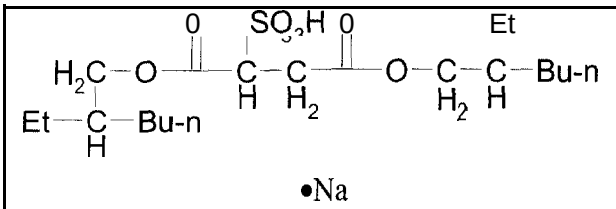
The Sulfosucccinates Category consists of three sulfosuccinate esters as designated above. The molecular structure of all three category members is essentially the same. The general structure for the category is defined as "dialkyl sodium sulfosuccinate" or "dicycloalkyl sodium sulfosuccinate." This describes a molecule with a succinic ester backbone, in which a carbon alpha to one of the carboxyl functions has a sodium sulfo group in place of a hydrogen atom. The only structural difference in the three substances is the alcohol moiety of the ester function. The different alcohol groups are 2-ethylhexyl-, cyclohexyl- and 1,3-dimethylbutyl. The generic molecular structure of all category members is shown below:

$ROOCCH_2CH(SO_3Na)COOR$, Where R = 2-ethylhexyl- $[CH_3(CH_2)_3CH(CH_2CH_3)-]$

= 1,3-dimethylbutyl- $[(CH_3)_2CHCH_2CH(CH_3)-]$

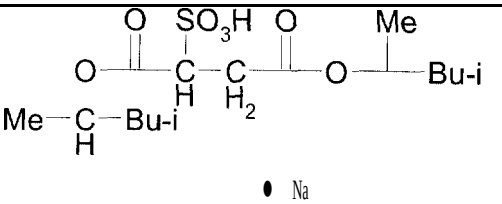
= cyclohexyl- [cyclic $-(CH_2)_5CH-$]

The structures are as follows:



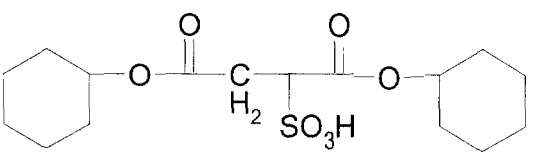
•Na

CAS 577-l 1-7



• Na

CAS 2373-38-8



•Na

CAS 23386-52-9

The three substances are grouped together because of their close structural relationships and the resulting similarities of their physiochemical and toxicological properties. The three sulfosuccinates that are proposed for the category can be used as surfactants or wetting agents, adjuvant in tablets, dispersing or emulsifying agents in foods, and as ingredients in some adhesives, polymeric coatings, detergents, cosmetics and vitamin preparations, They are marketed as solids or solutions in various alcohols.

The ethylhexyl ester is also known as dioctyl sodium sulfosuccinate or docusate sodium. It is generally regarded as safe when used as a stool softener and when used to lower surface tension and produce a mucolytic effect. The usual dosage for these indications is 50 to 2.50 mg daily for adults and children over 12, and 50 to 150 mg for children aged 2-12 (AMA, 1983). As of March 1994, dioctyl sodium sulfosuccinate was reported to be used in 44 cosmetic formulations (FDA, 1994). Concentrations of use are no longer reported to the FDA (Federal Register, 1992). However, FDA data from 1984 report dioctyl sodium sulfosuccinate concentrations in a variety of cosmetics at $\leq$ 5% (FDA, 1984). Dioctyl sodium sulfosuccinate can be used up to 15 ppm in finished gelatin desserts, 10 ppm in finished beverages or fruit juice drinks, 25 ppm in molasses, 25 ppm in non-carbonated beverages containing cocoa fat, 0.5% by weight in gums and hydrophilic colloids, and 9 ppm in finished products when used as a diluent in color additive mixtures for food (CFR, 2000; CIR, 1996).

2.3 Chemical Reactivity and Metabolism

The category members are all chemically stable at room temperature and neutral conditions. They are not particularly sensitive to oxidation, except in the presence of strong oxidizers. They are stable for long periods in aqueous systems, but are expected to undergo saponification (cleavage of the ester groups) in the presence of strong base.

Metabolic studies in animals indicate that the ethylhexyl ester is absorbed and metabolized to some extent after oral administration. Within 24-48 hours of oral administration, 25-35% of ^{35}S-labeled, and 64.1% of ^{14}C-labeled ethylhexyl ester are excreted into urine of rats (Pate1 et al., 1969; Kelly, 1973). Up to 89% of an orally administered dose is excreted into urine of rabbits (Kelly, 1973). The metabolic profile in the rabbit suggests that it is absorbed intact rather than being hydrolyzed in the GI tract prior to absorption. In dogs, 25.5 % and 71 .1% of ^{14}C-labeled ethylhexyl ester is excreted into urine and feces, respectively, suggesting a lower degree of absorption in the dog than the rat (Kelly, 1973). In humans given 100 mg or 200 mg orally, dioctyl sodium sulfosuccinate is present in bile at concentrations of 2-4 x 10^{-5} M (Dujovne and Shoeman, 1972).

From 15.5 to 18.6 % of an orally administered dose (5 to 10 mg) of ^{14}C-labeled ethylhexyl ester to rats is excreted into urine as 2-ethylhexanol-forming compounds. In humans, excretion of 2-ethylhexanol into urine accounts for 2.5-5.0% of an administered dose (200 mg) (Kelly et al., 1973). Therefore, metabolism of the ethylhexyl ester to 2-ethylhexanol is not a major pathway of metabolism in humans.

Based on the data obtained for the ethylhexyl ester and the structural similarities between this chemical and the cyclohexyl and dimethylbutyl esters, it is likely that the cyclohexyl and dimethylbutyl esters are also absorbed to some extent after oral administration. However, since alkyl chains on either of these molecules do not contain the ethyl hexyl moiety, they will not be metabolized to 2-ethylhexanol.

3. Test Plan

3.1 Chemical and Physical Properties

All three category members can be considered organosulfo salts. As neat materials, therefore, they are solids with high melting points, negligible volatility (vapor pressure). When heated above 300" C, they will undergo decomposition instead of boiling. All members are slightly to very slightly soluble in water due to the presence of the sodium sulfo group, which enhances hydrophilicity. However, due to the presence of two 6- and 8-carbon alkyl groups in the ester function, water solubility is limited, and affinity to lipids and hydrophobic materials is enhanced. For this reason, solubility in aqueous media is enhanced by the added presence of water-miscible solvents such as low molecular weight alcohols. Chemical/physical properties are summarized in Table 1.

part solid, part liquid, and will go into solution if a water-miscible organic solvent is present. The solubility of ethylhexyl ester in water is 15 g/l at 25" C, 23 g/l at 40" C, 30 g/l at 50" C, and 55 g/l at 70" C (Windholz, 1983). Water solubility values supplied by the manufacturer for the cyclohexyl ester and dimethylbutyl ester at 25" C are 120 g/l and 300-320 g/l, respectively (Cytec Industries Inc., 2001).

3.1.6 Test Plan for Physical Properties

Pertinent physical property values have been determined either through measurement or estimations using models, such as EPIWIN. No additional determinations are needed.

3.2 Environmental Fate and Pathways

Results of environmental fate studies with the three sulfosuccinates are summarized in Table 2.

Table 2. Environmental fate studies with sulfosuccinates

Endpoint	Cyclohexyl ester, (CAS # 23386-52-9)	Dimethylbutyl ester, (CAS # 2373-38-8)	Ethylhexyl ester, (CAS # 577-l l-7)
Photolysis (Atmospheric $T_{1/2}$)	*5.2 hours*	*7.3 hours*	*5.6 hours*
Photolysis (Hydroxyl Radical Rate Constant)	*24.6 E-12 cm^3/molecule-sec*	*17.4 E-12 cm^3/molecule-sec*	*23.0 E-12 cm^3/molecule-sec*
Stability in Water	*I. 4.5 years @ pH8; 14.5 years @ pH7*	*15.6 years @ pH8; 156 years @ pH7*	*243 days @ pH 8; 6.7 yr @ pH7*
Biodegradation'	35.9% after 28 days (Shake flask)	40.3% after 28 days (Shake flask); 16.7% after 28 days (Closed bottle)	66.7% after 28 days (Closed bottle)
Koc	111	*57.6*	*1040*
Henry's Law Constant	*3.14E-13 atm-m^3/mole (EPI WIN)*	*1.61E-12 atm-m^3/mole (EPIWIN)*	*5.00E-12 atm-m^3/mole (EPIWIN)*

Italicized values are derived from EPIWIN model
'Biodegradation data are for a marketed form of dimethylbutyl ester containing 80% CAS # 2373-38-8, 15% water and 5% ethanol.

3.2.1 Photodegradation

The results of EPIWIN modeling (Table 2) indicate that all three sulfosuccinates are degraded by photolysis to a similar extent.

3.2.2 Stability in Water

The EPIWIN model predicts that these succinate salts are stable to hydrolysis in water with half-lives estimated at several years (Table 2). The dimethylbutyl ester is estimated to hydrolyze more slowly in water than the other sulfosuccinates.

3.2.3 Biodegradation

Results of experiments OECD guideline studies will all three sulfosucccinates also indicate moderate rates of biodegradation. Results of shake flask tests indicate 35.9% biodegradation of the cyclohexyl ester and 40.3% biodegradation of a marketed form of the dimethylbutyl ester after 28 days (United States Testing Company, Inc. 1988a,b). The closed bottle (United States Testing Company, Inc., 199 1 a) test indicates a lower rate of biodegradation of a marketed form of the dimethylbutyl ester (16.7%) than the shake flask test (40.3%). The ethylhexyl ester had a higher rate of biodegradation than the other two sulfosuccinates (66.7% by 28 days in the closed bottle test)(United States Testing Company, Inc., 199 1 b).

A study by Vrbanova et al. (1999) suggests that the initial rates of biodegradation of sulfosuccinate esters increases with increasing length of the alkyl chain up to the C-8 ester, and that the substitution of cyclohexyl for n-hexyl results in a 4-fold decrease in the rate of biodegradation (Vrbanova et al., 1999). Further analyses revealed that the primary factors influencing the rate of biodegradation of linear sulfosuccinates are the number of carbons on the chain (rather than branching) and the degree of hydrophobicity (surfactants with medium hydrophobicity decompose more rapidly than the highly hydrophobic or hydrophilic ones). Based on this analysis, the cyclohexyl and dimethylbutyl esters should degrade more slowly than the ethylhexyl ester. Results of the OECD studies confirm this relationship.

3.2.4 Fugacity

The Mackay Level III fugacity model allows the estimation of relative distributions of chemicals released into the environment, but does not predict actual environmental concentrations. Distributive models, such as the MacKay Level III model, assume zero loss of material through degradation or dispersion out of the environmental system. The MacKay Level III model predicts that all three succinate salts will partition primarily to soil/sediment, some to water and a negligible portion to air (Table 3).

Table 3. MacKay Level III fugacity model

Medium	Cyclohexyl ester (CAS # 23386-52-9)	Dimethylbutyl ester (CAS # 2373-38-8)	Ethylhexyl ester (CAS # 577-l l-7)
	Concentration %	Concentration %	Concentration %
Air	0.875	0.00111	0.287
Water	40.18	27	15.5
Soil	58.2	71.4	46.8
Sediment	0.1	1.68	37.4

The ethylhexyl ester is predicted to partition more to sediment and less to water than the other esters. This is in agreement with the relatively high estimated K_{oc} value of 1040 given in Table 2 for the ethylhexyl ester, as compared with the other two category members. The dimethyl butyl ester is more likely to partition to soil. The very low predicted air concentrations are in agreement with the known negligible volatility of the sulfosuccinate salts, and the low values estimated for the Henry's Law Constants.

3.2.5 Test Plan for Environmental Fate Parameters

All endpoints have been met by experimentation or use of EPIWIN. No further testing is required.

3.3 Ecotoxicity

Results of ecotoxicity studies with the three sulfosuccinates are summarized in Table 4.

Table 4. Ecotoxicity Studies with Sulfosuccinates

Endpoint	Cyclohexyl ester, (CAS # 23386-52-9)	Dimethylbutyl ester, (CAS # 2373-38-8)	Ethylhexyl ester, (CAS # 577-l l-7)
Acute toxicity to fish	96 hr LC_{50} (bluegill) = 470 mg/l	96 hr LC_{50} (bluegill, trout) > 1000 mg/l; 1200 mg/l	96 hr LC_{50} (bluegill, trout) = 37 mg/l; 28 mg/l
Acute toxicity to Daphnia	48 hr EC_{50} = 457 mg/l	ND	48 hr EC_{50} = 36.2 mg/l
Toxicity to algae	No EC_{50} determined Growth stimulated	ND	ND
Phytotoxicity	NOEL (24, 48 hr) =10 mmol/l; 1.25 mmol/l	ND	NOEL (24, 48 hr) = 0.625 mmol/l; < 0.3125 mmol/l
Bioconcentration Factor (BCF)	3.162	3.162	*1.750*

ND = not determined experimentally. Fish toxicity data for the dimethylhutyl ester are for a marketed form containing 80% CAS # 2373-38-8, 15% water and 5% ethanol.
Italicized values designate values obtained by EPIWIN

3.3.1 Acute Toxicity to Fish

Acute toxicity studies in fish have been performed for all three sulfosuccinates. The LC_{50} values for the ethylhexyl ester in two different species of fish range from 28- 37 mg/l (Analytical Biochemistry Laboratories, 1987a, Goodrich et al., 199 1; Goodrich/Huber/Lech, 1985; United States Testing Company, 1990a). The LC_{50} value for the cyclohexyl ester is approximately one order of magnitude higher (470 mg/l)(Analytical Biochemistry Laboratories, 1987b), and the LC_{50} value for a marketed form of the dimethylbutyl ester in two different species is

approximately 1000 g/l (Analytical Biochemistry Laboratories, 1987c; United States Testing Company, Inc. 1990b). The range of LC_{50} values for the sulfosuccinates correlates roughly with the length of side chain.

3.3.2 Acute Toxicity to Aquatic Invertebrates

Data are available for two of the sulfosuccinates (ethylhexyl and cyclohexyl)(GoodrichLech, 1985; Exxon Biomedical Sciences, Inc. 1993a). The 4%hour EC_{50} values for effects on Daphnia for the ethylhexyl ester (36.2 mg/l) and the cyclohexyl ester (457 mg/l) do not differ significantly from their corresponding 96 hr-LC_{50} values determined for fish. Therefore, it is expected that the 48-hour EC_{50} value for exposure of Daphnia to the dimethylbutyl ester would be similar to its 96 hr-LC_{50} value for fish (approximately 1000 mg/l).

3.3.3 Acute Toxicity to Aquatic Plants

Algal toxicity data are available for the cyclohexyl ester. Incubation of Selenastrum capricornutum with 90 mg/l cyclohexyl ester stimulates for 96 hours stimulates growth by 243% (Exxon Biomedical Sciences, Inc, 1993b). Based on the structural similarities between the sulfosuccinates, it is expected that the sodium salts of the ethylhexyl and the dimethylbutyl esters would also stimulate algal growth.

3.3.4 Acute Toxicity to Terrestrial Plants

Data are available for two of the sulfosuccinates (ethylhexyl and cyclohexyl). The toxicity of these sulfosuccinates to Tradescantia bicolor (Wandering Jew) follows the same type of relationship as was observed with fish and Daphnia – the ethylhexyl ester is more toxic (NOEL (48 hr) < 0.3 125 mmol/l) than the cyclohexyl ester (NOEL (48 hr) = 1.25 mmol/l)(Oros et al. 1999). Analyses that Oros and coworkers made with several sulfosuccinic acid esters showed that by decreasing the lipophilicity of the molecules, cyclization and branching of the alkyl chain decreased the toxicity.

3.3.5 Other

The bioconcentration factors (BCF) of the three sulfosuccinates are estimated to range from 1.75 to 3.16, indicating a low potential to bioconcentrate.

3.3.6 Test Plan for Ecotoxicity

No new ecotoxicity testing is recommended. Fish toxicity studies have been performed with ail three sulfosuccinates. Based on the structural similarities of the molecules and the weight of the evidence, the algal and Dapbnia toxicity studies that have been performed on one or two of the sulfosuccinates should suffice for all three.

3.4 Human Health Data

Results of mammalian toxicity tests are summarized in Table 5.

Table 5. Mammalian toxicity of sulfosuccinates

Endpoint	Cyclohexyl ester, (CAS # 23386-52-9)	Dimethylbutyl ester, (CAS # 2373-38-8)	Ethylhexyl ester, (CAS # 577-11-7)'
Acute oral	LD_{50}(rat) = 3.54 g/kg[2]	LD_{50}(rat) = 1.75 g/kg[2]	LD_{50}(rat) = 2 g/kg; 3.08 g/kg; 4.2 g/kg LD_{50}(mouse) = 2.643 g/kg; 4.8 g/kg
Acute dermal	LD_{50}(rabbit) > 5 g/kg[2]	LD_{50}(rabbit) = 5 ml/kg[2] (4 g/kg as contained solids)	LD_{50} (rabbit) > 10 g/kg
Repeated dose (32 day)	NOEL(rat) > 1 .0%[2]	NOEC(rat) > 0.5 %[2]	ND
(90 day)	NOEL(oral rat) > 1 .0% dietarv	NOEL(oral rat) > 1 .0% dietary	NOEL (oral rat) > 1.0% dietary
(16 weeks)	ND	ND	NOEL (oral feed) < 2% dietarv
(26 weeks)	ND	ND	NOEL (oral rat) = 0.5% dietary; LOEL (oral rat) = 1 .O% dietary
(1 year)	ND	ND	NOEL (oral beagle) = 30 mg/kg
Genetic toxicity (in vitro)	Ames test - negative	ND	Ames test - negative CHO cells - positive only at cytotoxic conc.
Carcinogenicity	ND	ND	NOEL (oral rat) = 0.5% dietary; LOEL (oral rat) = 1 .O% dietary; reduced weight gain
Reproductive toxicity	NOEL (oral rat) > 1 .O% dietary for reproductive organs	NOEL (oral rat) > 1 .0% dietary for reproductive organs	NOEL (oral rat) = > 1% dietary for reproductive organs; 1 .0% dietary for reproductive effects; < 0.5% dietary for lactation
Developmental toxicity	ND	ND	NOEL (oral rat) = 1.0% dietary; LOEL (oral rat) = 2.0% dietarv

ND = not determined

'Also referred to as dioctyl sodium sulfosuccinate. Data are reported from studies that used "dioctyl sodium sulfosuccinate", but not "n-dioctyl sodium sulfosuccinate"

[2]A marketed form of the material containing 80% CAS # and 6-8% ethanol was used in the study

3.4.1 Acute Toxicity

Oral LD_{50} values have been reported for all three chemicals in the category (dimethylbutyl as marketed form). In rats, the oral LD_{50} values range from 1.75 - 4.2 g/kg, indicating a low degree of oral acute toxicity (American Cyanamid, 1957, 1966, 1969; Olson et al., 1962; Huntingdon Research Center, 1977). Values obtained in mice (2.6 - 4.3 g/kg) (Hopper et al., 1949; Case et al., 1977) and rats (2 - 4.2 g/kg) for the ethylhexyl ester are similar. There is no significant difference between the LD_{50} values for all three compounds, indicating a similar degree of acute oral toxicity.

Dermal LD_{50} values also have been reported for all three chemicals in the category. The values range from 5 ml/kg (4 g/kg) for a marketed form of the dimethylbutyl ester, to > 10 g/kg for the ethylhexyl ester, indicating a low degree of dermal acute toxicity (American Cyanamid, 1957, 1969; Huntingdon Research Center, 1977; Vernon et al. 1990).

3.4.2 Repeated Dose Toxicity

Oral repeated dose toxicity studies have been performed on all three sulfosuccinates. Results of 32-day studies in rats indicate a NOEL of ≥ 1.0% for the cyclohexyl ester and ≥ 0.5% for the marketed form of the dimethylbutyl ester (American Cyanamid, 1957, 1969). The results of 90-day studies in rats indicate NOELs of ≥ 1% dietary for all three sulfosuccinates (Industrial Bio-Test Laboratories, 1969). Longer term oral toxicity studies in rats (16 or 26 weeks) have shown NOELs of < 2% and 0.5%, respectively (Fitzhugh 1948; Taylor 1966). The only effects noted in rats treated with 2% for up to 26 weeks were GI irritation and reduced weight gain. Daily oral administration of 30 mg/kg ethylhexyl ester for 1 year produces no adverse effects in dogs (Case et al., 1977). Taken together, these results suggest that all three sulfosuccinates are fairly well tolerated when administered repeatedly.

3.4.3 Genetic Toxicity

The cyclohexyl ester has been tested for mutagenicity in Salmonella strains TA-98, TA-100, TA- 1530, TA-1535, TA 1538 and WP-2uvrA- in the absence of S9 (American Cyanamid, 1976), and the ethylhexyl ester has been tested in strains TA-98, TA-100, TA-102, TA-1535, TA-1537 and TA- 1538 in the absence and presence of S9 (Bonin and Baker, 1980; Hazelton Microtest, 1993a). The ethylhexyl ester was tested at the highest concentrations that did not produce cytotoxicity. Results of both studies were negative. A chromosomal aberration assay in Chinese Hamster Ovary cells (CHO) has been conducted with the ethylhexyl ester (Hazelton Microtest, 1993b) . In one out of three experiments, 120 micrograms/ml ethylhexyl ester induced significant chromosomal aberrations (241100 cells scored) in the presence of S-9 activation. The majority were abnormalities other than chromosomal gaps. Toxicity at the concentration that produced aberrations (120 µg/ml) was demonstrated as a 62% reduction in mitotic activity. Complete toxicity at doses exceeding 140 µg/ml was observed. In summary, the ethylhexyl ester only produced aberrations at a concentration close to the toxic threshold.

3.4.4 Carcinogenicity

Long-term studies (up to 2 years) in rats with the ethylhexyl ester have shown that a dietary concentration of 1% produces no adverse effects except reduced weight gain (Fitzhugh and Nelson, 1948). Gastrointestinal irritation is noted in rats ingesting 2% ethylhexyl ester in the diet for 2 years, and ingestion of 8% produces severe GI irritation and lethality within a week (Fitzhugh and Nelson, 1948).

3.4.5 Reproductive Toxicity

Two three-generation reproductive toxicity experiments of have been performed on the ethylhexyl ester (American Cyanamid, 1970; Hazleton Laboratories, 1986; Mackenzie et al., 1990). In each of the experiments, a dietary level of 0.5% was shown to affect parental food consumption, parental and fetal body weight of most generations. However, doses of up to 1 .0% had no effect on fertility and gestation. Ingestion of 2.0% ethylhexyl ester in the diet on days 6-16 of gestation is associated with growth retardation in dams and a significant increase in fetal resorptions (Hoechst Roussel, 1976, 1979). In the reproductive toxicity study by American Cyanamid (1970), ingestion of 1% was associated with decreased lactation index of FO and F2 dams and survivability of the F3 generation. In this study, test diet of some of the dams was replaced with regular diet just prior delivery and during lactation, and their offspring were placed on test diets after weaning. With the exception of the Flb pups, no effects of up to 1 .0% ethylhexyl ester on viability, mean weight, or lactation were noted in pups from dams that did not receive DSS during lactation. This suggests that either the ability of dams to produce milk or the taste of the milk was affected by ingestion of ethylhexyl sulfosuccinate during lactation. Evidence to support this hypothesis comes from the finding in the Hazleton study (wherein all dams were given test diet during lactation) of dose-dependent increases in the number of pups with no milk in their stomachs.

Results of 90-day studies show that ingestion of up to 1 .0% of any of the sulfosuccinates in the category has no effect on reproductive organs of male or female rats (Industrial Bio-Test Laboratories, 1969). The fact that decreased weight gain or food consumption were not noted in rats treated with up to 1 .0% dimethylbutyl or cyclohexyl esters in the diets for 90 days indicates that, unlike the ethylhexyl ester, issues associated with palability (i.e. reduced weight gain in dams and lactation in pups) are not likely to be caused by these compounds at this concentration.

3.4.6 Developmental Toxicity

In the three generation reproductive toxicity studies mentioned above, no developmental toxicity was observed in pups born of rats treated with ethylhexyl ester at concentrations up to 1 .0% (American Cyanamid, 1970; Hazleton Laboratories, 1986; Mackenzie et al., 1990). No adverse effects are noted in offspring of rats given 1 .0% ethylhexyl ester in the diet on days 6-l 5 of gestation (Hoechst Roussel, 1976). Ingestion of 2.0% ethylhexyl ester in the diet on days 6-15 of gestation is associated with an increased percentage of malformed fetuses (20% versus 0% in controls (Hoechst Roussel, 1976). Abnormalities in fetuses include exencephaly, spina bifida, microphthalmia, curved or open vertebral columns, and incomplete ossification of various

cranial bones. An additional study performed at 2.0% also indicates that this dose is associated with an increase in skeletal abnormalities (Hoechst Roussel, 1979; Mattison, 1984). The effects noted at this concentration are associated with maternal toxicity as evidenced by growth retardation and a significant increase in fetal resorptions. Based on the available data and the structural similarities of the compounds, it can be surmised that the cyclohexyl and dimethylbutyl esters would also produce maternal and subsequent developmental toxicity at **2.0%.**

3.4.7 Human Experience

A retrospective study on drug use of 6,837 women during pregnancy indicates that use of dioctyl sodium sulfosuccinate during pregnancy is not associated with an increased risk of birth defects in offspring (Jick et al., 1981).

3.4.8 Test Plan for Mammalian Toxicity

Based on the structural similarities of the molecules and the flat repeated dose mammalian toxicity profile for all three sulfosuccinates, tests already performed will be predictive of results for the other sulfosuccinates.

3.5 Conclusion

Physical Properties

As stated in Section 2.2, the three chemical substances that comprise the Sulfosuccinates Category all have a common molecular structure. Each category member has a molecular structure that consists of a succinic ester backbone, in which a carbon alpha to one of the carboxyl functions has a sodium sulfo group in place of a hydrogen atom. The only structural difference in the three substances is the alcohol moiety of the ester functions. The different alcohol groups are 2-ethylhexyl-, cyclohexyl- and 1,3-dimethylbutyl-.

All three category members have similar physical properties. As neat materials they are all solid salts with high melting points, and negligible vapor pressure. Because they are salts, they will degrade when heated to high temperatures (>300° C) and not boil.

Environmental Fate

All three category members are predicted to undergo photolysis in the atmosphere, with half lives estimated to range from 5.2-7.3 hours. All members are predicted to be stable to hydrolysis in neutral water, but will undergo cleavage of the ester group in the presence of strong base. Biodegradation studies indicated that the succinate esters biodegrade at moderate rates. The Log Kows are estimated at 1.76 for the cyclohexyl ester, 3.98 for the dimethyl butyl ester, and 6.10 for the ethylhexyl ester, which correlate roughly with increasing chain length of the alkyl ester group. Water solubility tends to decrease with increasing side chain length, while Koc values (which predict soil mobility) tend to increase with chain length. Thus, the 2-ethylhexyl ester

appears to be the least water soluble, to have the greatest lipophilicity, and (with the highest Koc value) appears to have the least mobility in soil. The predicted Henry's Law constants for the three sulfosuccinates are low (<1 E-8 atm-m^3/mole). That is consistent with the negligible vapor pressure of salts,

The MacKay Level III fugacity model predicts a similar relative environmental distribution for all three category members, indicating negligible distribution to air, moderate distribution to water, and high distribution to soil and sediment.

Ecotoxicity

The ethylhexyl ester is more toxic to aquatic species than the cyclohexyl ester. Based on studies which indicate that the ecotoxicity of the sulfosuccinates is governed by the length of the side chain, the dimethylbutyl ester is expected to behave more like the cyclohexyl ester than the ethylhexyl ester. The bioconcentration factor (BCF) of the three sulfosuccinates are estimated to range from 1.75 to 3.16, indicating a low potential to bioconcentrate.

Mammalian Toxicity

Results of 90-day repeated dose oral toxicity experiments indicate NOELs of > 1 .O% for all three sulfosuccinates. Based on the structural similarities of the molecules and a flat repeated dose toxicity profile, most tests performed on the ethylhexyl ester will be predictive of results for the other sulfosuccinates. It is likely that the inhibition of lactation caused by the ethylhexyl ester at 1 .0% will not be observed with the dicyclohexyl and dimethylbutyl esters because they do not appear to be unpalatable at this concentration.

Summary

In summary, the data provided in the robust summaries and test plan are consistent with the close molecular similarity and identical functional groups of the category members. The data confirm the validity of the Sulfosuccinates Category. No new testing is required.

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5. Appendix 1 - Criteria for listing of robust summaries

Robust summaries for all HPV endpoints were written from all available data with the following exceptions:

Ethylhexyl ester (CAS #577-11-7) - A biodegradation study by Hammerton (1955) was not summarized because its conduct would not meet today's standards. Toxicity studies performed by Benaglia et al (1943) on rats, rabbits, monkeys and dogs and were not summarized because the results were not well documented, the number of animals was not sufficient, or the NOEL was difficult to determine. Results of a study by Hopper et al. (1949) in mice (LD_{50} = 4.8 g/kg) also were not summarized because the conduct of the study would not be acceptable by today's standards. Physical chemistry and fish toxicity data (48 hr LC_{50} in killifish of 6 1.3 mg/l) from CITI also were not included because the primary source of information was unknown. All studies described in these references would be assigned a reliabiiity of 3 (based on the standards of Klimisch et al., 1997).

6. Appendix 2 - Robust Summaries

AR201-13133B

IUCLID

Data Set

Existing Chemical : Butanedioic acid, sulfo-1,4-bis(1,3-dimethylbutyl) ester, sodium salt
CAS No. : 2373-38-8

Printing date : 30.04.2001

1. General Information

Id 2373-38-8
Date 30.04.2001

1.2 SYNONYMS

Succinic acid, sulfo-1,4-bis(1,3-dimethylbutyl)ester, sodium salt

2.1 MELTING POINT

Value	ca. 87.4 - 133.2" C
Method	other (calculated)
Year	2000
GLP	not applicable for estimations
Test substance	succinic acid, sulfo-1,4-bis(1,3-dimethylbutyl)ester, sodium salt
Remark	The melting point was estimated by the EPIWIN model, based on molecular structure and functionality.
Reliability	(2) valid with restrictions. Data were obtained by modeling.

03.03.2001

2.2 BOILING POINT

Value	> 300" C at 750 mm Hg
Decomposition	**yes**
Method	other (calculated)
Year	2000
GLP	not applicable for estimations
Test substance	succinic acid, sulfo-1 ,4-bis(1,3-dimethylbutyl)ester, sodium salt
Remark	The substance is a salt with negligible volatility. It undergoes decomposition before boiling when heated. The boiling point of 661.8" C was derived using the EPIWIN model, based on an adapted Stein and Brown Method.
Reliability	(3) invalid. Material will decompose before boiling.

03.03.2001

2.4 VAPOUR PRESSURE

Value	< .000001 hPa at 25" C
Method	other (calculated)
Year	2000
GLP	not applicable for estimations
Test substance	succinic acid, sulfo-1,4-bis(1,3-dimethylbutyl)ester, sodium salt
Remark	The vapor pressure was estimated from the melting point using the EPIWIN model. The substance is not volatile, since it is a salt.
Reliability	(2) valid with restrictions. Data were obtained by modeling.

03.03.2001

2.5 PARTITION COEFFICIENT

Log Pow	ca. 3.98 at 25" C
Method	other (calculated)
Year	2000
GLP	not applicable for estimations
Test substance	succinic acid, sulfo-1,4-bis(1,3-dimethylbutyl)ester, sodium salt
Remark	The log Pow was calculated using the EPIWIN model, based on molecular

structure and functionality.

Reliability : (2) valid with restrictions. Data were obtained by modeling.
03.03.2001

2.6.1 WATER SOLUBILITY

Value : ca. 30-32 g/1 00 ml at 25" C
Method : no data
Year : 2001
GLP : no data
Test substance : succinic acid, sulfo-1,4-bis(1,3-dimethylbutyl)ester, sodium salt

Remark : Data were supplied by the manufacturer.

Reliability : (2) valid with restrictions. Details on how value was obtained are unknown
03.03.2001 (3)

3.1.1 PHOTODEGRADATION

Type	: air
Light source	: sun light
Light spect.	nm
Rel. intensity	based on Intensity of Sunlight
Direct photolysis	
Halflife t1/2	: ca. 7.3 hour(s)
Method	: other (calculated)
Year	: 2000
GLP	: not applicable for estimations
Test substance	: succinic acid, sulfo-1,4-bis(1,3-dimethylbutyl)ester, sodium salt
Remark	: The half-life and rate constant at 25°C were estimated using the EPIWIN/AOPWIN model that estimates the rate constant for the atmospheric gas-phase reaction between photochemically produced hydroxyl radicals and ozone with organic chemicals. The rate constant estimated by the program was used to calculate the atmospheric half-life based upon the average atmospheric concentration of hydroxyl radicals.
Result	: The hydroxyl radical photolysis rate constant was calculated to be 17.4 E-12 cm^3/molecule-sec.
Reliability	: (2) valid with restrictions. Data were obtained by modeling.
03.03.2001	

3.1.2 STABILITY IN WATER

Type	: other:estimation
t1/2 pH7	: ca. 156 years at 25" C
t1/2 pH 8	: ca. 15.6 years at 25" C
Deg. Product	: not determined
Method	: other (calculated)
Year	: 2000
GLP	: not applicable for estimations
Test substance	: succinic acid, sulfo-1,4-bis(1,3-dimethylbutyl)ester, sodium salt
Remark	: Half-lives were calculated using the EPIWIN/HYDROWIN program based on molecular structure and functionality.
Reliability	: (2) valid with restrictions. Data were obtained by modeling.
03.03.2001	

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	: volatility
Media	: water – air
Air (level III)	: .0011
Water (level III)	: 27
Soil (level III)	: 73
Method	: other
Year	: 2000
Test substance	: succinic acid, sulfo-1,4-bis(1,3-dimethylbutyl)ester, sodium salt
Remark	: Level III Fugacity was estimated using the Mackay model (the currently

accepted model for estimation of theoretical distribution) with standard defaults contained in Syracuse Research Center EPIWIN program, The 73% indicated for soil is actually 71.3% in soil and 1.7% in sediment.

Result : A Henry's Law Constant of 1.61 E -12 atm-m^3/mol was calculated, based on molecular structure and functionality. The Koc was estimated by the EPIWIN model to be 57.6. The Koc value indicates limited mobility in soil.

Reliability : (2) valid with restrictions. Data were obtained by modeling.
03.03.2001

3.5 BIODEGRADATION

Type : aerobic
Inoculum : activated sludge
Contact time : 28 day
Degradation : = 40.3 % after 2% day
Result : not readily biodegradable
Kinetic of test substance : 14 day 50 %
21 day 38 %
28 day 40.3 %
Control substance : aniline
Kinetic : 14 day 90%
21 day 87%
28 day 86.7 %
Method : OECD Guide-line 301 E "Ready biodegradability: Modified OECD Screening Test"
Year : 1988
GLP : yes
Test substance : other TS

Result : The amount of biodegradation observed occurred within the first seven days of the test and remained constant for the remainder of the study. The reference material yielded a degradation percentage over 80%, so the results of this test are therefore considered valid.

Test condition : Testing was conducted in accordance with a modified OECD Screening Test for Ready Biodegradability. Activated sludge bacteria was from Bergen Co., New Jersey. The test compound was dissolved in an organic medium at a concentration of 30.8 mg/ml. The medium was inoculated with a relatively low concentration of microorganisms from a mixed population and aerated at a temperature of 20-25" C for a period of 28 days. Biodegradation was followed by dissolved organic carbon (DOC) analysis. Positive control flasks containing aniline (30.8 mg/l) were run parallel to determine the validity of the test. The amount of DOC reduction in blank controls was subtracted from values obtained for the test material and positive control to obtain the final values.

Test substance : Test material was 80% CAS #2373-38-8, 15% water, 5% ethyl alcohol. It was identified as 68% carbon by analysis.

Reliability : (1) valid without restriction
03.03.2001 (5)

Type : aerobic
Inoculum : activated sludge
Contact time : 28 day
Degradation : = 16.2 % after 28 day

Result	: not readily biodegradable
Kinetic of test substance	: see result
Control substance	: aniline
Kinetic	: 15 day 66.7 %
	28 day 98.1 %
Deg. **Product**	: not measured
Method	: OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
Year	: 1991
GLP	: **yes**
Test substance	: other TS

Remark: : The percent degradation listed above is average of two determinations with 2 mg/l material and one determination with 1 mg/l material.

Result : Duplicate tests performed with 2 mg/l test material revealed 0 and 2.9% degradation by day 5, 20.4% and 12.6 degradation by day 15, and 16.7 and 13.3% degradation by day 28. Test material at 1 mg/l degraded by 7.4%, 25.9%, and 18.5% over 5, 15, and 28 days, respectively. Aniline degraded by 18.5%, 66.7% and 98.1% over 5, 15, and 28 days, respectively. The test was therefore considered valid. The test material was not readily biodegradable.

Test condition : Testing was done in accordance with the OECD "Ready Biodegradability: Closed Bottle Test". The stock solution was prepared by adding 2 g of sample to 1 liter of distilled water. This solution was diluted to 100 ppm as carbon after analysis. The diluted stock was added to BOD bottles at 3.33, 6.67 and 16.65 ml to yield test concentrations of 1, 2 and 5 mg/l (as carbon, respectively). Aniline (2 mg/l) was used as a reference. The test and reference solutions were inoculated with microorganisms from a mixed population (activated sludge material from Bergen Co., New Jersey) and kept in closed bottles in the dark at a constant temperature of 20 +/- 1 ° C. Degradation was followed by oxygen analyses using the YSI Dissolved Oxygen analyzer 54A over a 28-day period. Degradability was based on a comparison between readings of actual oxygen demand to theoretically expected oxygen demand. Results were adjusted for blanks without inoculum.

Test substance : Test material was 78-80% CAS #2373-38-8, 15% water, 5% ethyl alcohol, less than 1.0% $C_6H_{14}O$, less than 0.5% $C_{16}H_{28}O_4$ and $H_20_4S.2Na$, 0.25% CH_4O, and less than 0.2% $H_2O_3S.Na$. It was verified as containing the same carbon content (68%) as identified by the supplier.

Reliability : (1) valid without restriction
03.03.2001

(7)

3.7 BIOACCUMULATION

Species	: other
BCF	: ca. 3.16 at 25" C
Method	: other: calculated
Year	: 2000
GLP	: not applicable for estimations
Test substance	: succinic acid, sulfo-1,4-bis(1,3-dimethylbutyl)ester, sodium salt

Remark : The bioconcentration factor was estimated based on molecular structure and functionality using the EPIWIN/BCF program.

Reliability : (2) valid with restrictions. Data were obtained by modeling.
04.03.2001

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	: static
Species	: Oncorhynchus mykiss (Fish, fresh water)
Exposure period	: 96 hour(s)
Unit	: g/l
Analytical monitoring	: no data
LC50	: c = 1200
LC100	: m = 2000
Method	: OECD Guide-line 203 “Fish, Acute Toxicity Test”
Year	: 1990
GLP	: no data
Test substance	: other TS

Remark : An initial range finding test was performed to determine the optimal concentrations for the test

Result : Water conditions: Dissolved oxygen and pH ranged between 8.8-9.6 mg/l and 7.0-7.7 units, respectively. There was no difference between groups. Conductivity increased in a dose-dependent manner, with control values at approximately 200 µmohs and 4000 ppm values at 550 µmohs. Temperature was maintained at 15” C throughout the test. Alkalinity and water hardness were 80 and 90 mg/l $CaCO_3$, respectively.

Test Results: None of the fish exposed to 0 (control), 250 or 500 ppm died by 96 hours. The corresponding mortalities at 96 hours for fish exposed to 1000, 2000, and 4000 ppm were 10, 100, and 100%, respectively. Most of the deaths that occurred at these concentrations occurred within 24 hours.

Test condition : This 96-hour static, non-renewal bioassay was performed on six groups of 10 Onchorhyncus mykiss (rainbow trout) approximately 74 days old. Trout were housed (5 per tank) in 4L polypropylene vessels containing 3 L of US EPA moderately hard, reconstituted water. The test concentrations were 0 (control), 250, 500, 1000, 2000, and 4000 ppm. Tests were performed in duplicate. Fish were maintained at 15 ± 2 °C under a 16hr/8hr light/dark cycle and were not fed during tests. Oil-free air was supplied at less than or equal to 100 bubbles per minute to maintain equal to or greater than 60% saturation. Mortality, behavior, physiology, dissolved oxygen, pH, and conductivity were measured initially and daily thereafter. Initial alkalinity and hardness of diluent were also determined. The test was considered valid if greater than 90% of control fish survived 96 hours.

Data were analyzed according to the Spearman-Karber method, Probit analysis, or graphical interpolation (where applicable).

Test substance : Test material was 80% CAS # 2373-38-8, 15% water, 5% ethyl alcohol

Reliability : (1) valid without restriction
03.03.2001 (6)

Type	: static
Species	: Lepomis macrochirus (Fish, fresh water)
Exposure period	: 96 hour(s)
Unit	: mg/l
Analytical monitoring	: no data
NOEC	: m = 560
LC50	: m > 1000

4. Ecotoxicity

Id 2373-38-8
Date 30.04.2001

Method : OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year : 1987
GLP : yes
Test substance : other TS

Result

None of the fish exposed to concentrations <= 560 mg/l died after 96 hours of exposure. Mortality of those exposed to 1000 mg/l was 10%. Water temperature and pH were maintained within acceptable limits for all tanks. A dose- and time -dependent decrease in dissolved O_2 was noted: it ranged from 6.4 (control) to 3.1 mg/l (560 and 1000 mg/l) at 48 hours and 5.9 (control) to 2.0 mg/l (1000 mg/l) at 96 hours. All solutions containing 100 to 1000 mg/l test material were slightly cloudy at 48, 72 and 96 hours. The NOEC was 560 mg/l based on the lack of mortality and abnormal effects

Test condition

Bluegill sunfish (Lepomis macrochirus) were acclimated for at least 14 days prior to test. They were fed a standard commercial fish food occasionally supplemented with brine shrimp daily until 48-96 hours prior to testing. A 96-hour static bioassay was conducted on the fish at the following nominal test concentrations 0 (control), 100, 180, 320, 560, and 1000 mg/l. Fish weighed an average of 0.30 g and had a mean length of 24 mm. The test material **was** tested on an as is basis and was not corrected for solids content. Ten fish were exposed per group. The tests were conducted in five-gallon tanks containing 15 l of reconstituted water. The water was prepared to yield a total hardness of 40-48 mg as $CaCO_3$, total alkalinity of 25-35 mg/l as $CaCO_3$ and an initial pH of 7.2 to 7.6. Tanks were maintained at 22 +/- 1° C and were not aerated. Water quality parameters of temperature, dissolved oxygen, and pH were measured throughout the test. Fish were observed every 24 hours for abnormal effects and lethality.

Data were analyzed according to a computerized LC_{50} program, which utilized the binomial, moving average and probit tests.

Test substance : The test material was 80% CAS # 2373-38-8, 15% H20, 5% ethanol. Purity was not specified.

Reliability : (2) valid with restrictions. Results at the high concentrations may have been confounded by low dissolved oxygen concentration and insolubility of test material.

03.03.2001 (2)

5.1.1 ACUTE ORAL TOXICITY

Type	: LD50
Species	: rat
Strain	: other:albino
Sex	: male
Number of animals	: 20
Vehicle	: water
Value	: = 1750 mg/kg bw
Method	: other
Year	: 1957
GLP	: pre-GLP
Test substance	: other TS

Result : All animals died within 24 hours following 2.5 g/kg dose, but all survived treatment with the lower doses. Animals exposed to 2.5 g/kg exhibited profound depression and severe diarrhea prior to death. Moderate to severe irritation with hemorrhage of the gastrointestinal tract was found on post-mortem examination. At the lower doses, the animals were depressed for 24 to 48 hours, but thereafter regained normal appearance and behavior. Autopsy of these animals revealed a greater than usual distention of the intestines in some instances, but otherwise no significant gross findings.

Test condition : Test material was administered in single doses by mouth to 4 groups of 5 young male albino rats at dosages ranging from 0.31 to 2.5 g/kg in terms of solids. Animals were observed for a period of 7 days, and then were sacrificed and autopsied. Animals that died before 7 days were autopsied upon death.

Test substance : Test material contained 80 +/- 1% active solids, 6-8% 2B ethanol, 0.4% sodium sulfate, 0.4% unreacted ester and a maximum of 10 ppm heavy metals. Test material was diluted with water to a solution of 5% solids content.

Reliability : (1) valid without restriction
03.03.2001 (1)

5.1.3 ACUTE DERMAL TOXICITY

Type	: LD50
Species	: rabbit
Strain	: other:albino
Sex	: male
Number of animals	: 12
Value	: = 4000 mglkg bw
Method	: other
Year	: 1957
GLP	: pre-GLP
Test substance	: other TS

Result : All animals exposed to 10 ml/kg died within one to three days following removal of the dose. Animals exposed to 10 ml/kg exhibited very severe erythema, edema, and necrosis of the skin and extreme depression prior to death. Post-mortem examination of these animals gave additional evidence of severe injury to the skin and abdominal wall. The mortality rate

of rabbits exposed to the two lower doses was 1/4. Erythema and edema were initially quite severe at the lower dosages, but the edema subsided within 24 to 48 hours Erythema persisted for 4 to 5 days. Autopsy of animals receiving '2.5 or 10 ml/kg revealed no gross internal pathology that could be related to administration of the product. The LD50 was 5.0 ml/ kg (4 g/kg as contained solids).

Test condition : The substance as received (containing 80% solids) was applied to the closely-clipped skin of male albino rabbits in single doses that remained in contact with skin for a 24-hour period. Four animals per group were exposed to 2.5, 5 or 10 ml/kg. The dose was retained by placing a cuff of polyethylene film around the trunk of each animal. Animals were observed for a period of 7 days, and then were sacrificed and autopsied. Animals that died before 7 days were autopsied upon death.

Test substance

Test material contained 80 +/- 1% active solids, 6-8% 2B ethanol, 0.4% sodium sulfate, 0.4% unreacted ester and a maximum of 10 ppm heavy metals

Reliability : (1) valid without restriction
03.03.2001 (1)

5.4 **REPEATED DOSE TOXICITY**

Species : rat
Sex : male
Strain : other: albino
Route of admin. : oral feed
Exposure period : 32 days
Post obs. period : none
Doses : 0.125, 0.25, 0.5%
Control group : **yes**
NOAEL : > .5 %
Method : other
Year : 1957
GLP : pre-GLP
Test substance : other TS

Result : Appearance and behavior of the animals over the study period were normal. None of the animals died. No pathology attributable to ingestion of the material was found

Test condition : The product was added to the diet of three groups of young male albino rats (ten/group), in amounts sufficient to give concentrations of 0, 0.125, 0.25, and 0.5% (solids content). Mean daily dosage of the product is calculated as 0, 0.13, 0.25, and 0.51 g/kg of solids for each percentage, respectively. These dietary levels were fed over a 32-day period. All animals were sacrificed and autopsied at the end of the study.

Test substance : Test material contained 80 +/- 1% active solids, 6-8% 2B ethanol, 0.4% sodium sulfate, 0.4% unreacted ester and a maximum of 10 ppm heavy metals.

Reliability : (1) valid without restriction
03.03.2001 (1)

Species : rat
Sex : male/female
Strain : other:Charles River albino
Route of admin. : oral feed

Exposure period	90 days
Post obs. period	**none**
Doses	1.0%
Control group	**no**
NOAEL	**> 1 %**
Method	other
Year	1969
GLP	pre-GLP
Test substance	other TS

Result

No deaths or abnormal behaviors were noted in the animals. No significant differences were noted in final body weights, food consumption, hematologies, urinalyses, or gross pathology (as compared to controls)

Test condition

Design: 20 albino rats / sex were fed test material for 90 days at a dietary concentration of 1 .0%, which was prepared by blending the appropriate amount of test material with standard rat ration. Twenty control rats/sex received normal food. Rats were weighed biweekly and food consumption was recorded weekly. Fresh diets were prepared weekly. Standard hematologies and urinalyses were performed on blood and urine samples collected from 5 rats/sex/group on treatment day 84.

Endpoints: Animals were sacrificed 90 days after treatment and a complete set of organs and other tissues was examined. At autopsy, the weight of the liver and kidneys of 10 rats/sex/group were recorded. The following tissues from 5 rats/sex/group were examined histologically:esophagus, stomach (cardia, fundus, pyloris), small intestine (duodenum, jejunum, ileum), cecum, colon , liver, kidneys, spleen, pancreas, urinary bladder, pituitary, adrenal, testes, seminal vesicle, ovary, bone marrow, thyroid, parathyroid, salivary gland, prostate, heart, aorta, lung, lymph node (cervical and mesenteric), skeletal muscle, peripheral nerve, bone (femur), spinal cord, uterus, trachea, eye, optic nerve and brain.

Statistical Analyses: Data for food consumption, weight, absolute organ weight and organ/body weight ratios were analyzed by analysis of variance (ANOVA). Effects uncovered were further analyzed by t-tests.

Test substance

A commercial sample was dried to remove the liquid phase. Dried product was 100% solids or active ingredients.

Reliability

(I) valid without restriction

02.03.2001

(4)

5.8 TOXICITY TO REPRODUCTION

Type	other: histological examination of reproductive organs
Species	rat
Sex	male/female
Strain	other:albino
Route of admin.	oral feed
Exposure period	90 days
Duration of test	90 days
Doses	1.0%
Control group	**yes**
Method	other
Year	1969
GLP	pre-GLP
Test substance	other TS

Remark

This study was a component of a 90-day repeated dose oral toxicity study.

Additional details about the conduct of this study can be found in section 5.4.

Result : No biologically significant changes were observed in any of the reproductive organs that were examined in males or females

Test condition : Diet was prepared by blending the appropriate amount of test material with standard rat ration. Twenty albino rats I sex were fed a diet containing 1 .O% test material for a period of 90 days. Animals were sacrificed 90 days after treatment and gross pathologies were performed. Ovaries and uteri from female rats and prostate, testes, and seminal vesicles from male rats were examined histopathologically.

Test substance : A commercial sample was dried to remove the liquid phase. Dried product was 100% solids or active ingredients.

Reliability : (1) valid without restriction
03.03.2001 (4)

6. References

Id 2373-38-8
Date 30.04.2001

(1) American Cyanamid Company. 1957. Report on Aerosol MA-80%. Limited Release Toxicity Studies. Report No. 57-15, October 7, 1957

(2) Analytical Biochemistry Laboratories, Inc. 1987. Report No. 36262 to American Cyanamid, October 29, 1987

(3) Cytec Research and Development. 2001. Unpublished information.

(4) Industrial BIO-TEST Laboratories, Inc. 1969. Ninety-day subacute oral toxicity of Aerosol A-196, Aerosol IB, Aerosol AY, Aerosol MA, Aerosol OT and Aerosol TR in albino rats. Report No. 87409 to American Cyanamid.

(5) United States Testing Company, Inc. 1988. OECD Screening test for ready biodegradability. Report No. 07278-4 to American Cyanamid, January 15, 1988

(6) United States Testing Company, Inc. 1990. Aquatic Toxicity tests versus Onchorhyncus mykiss. Report No. 063102-g to American Cyanamid Co, January 21, 1990

(7) United States Testing Company, Inc. 1991. OECD Screening test for ready biodegradability. Test Report No. 063012-12 to American Cyanamid, February 20, 1991.

I U C L I D

Data Set

New Chemical	: Butanedioic acid, sulfo-, 1,4-bis(2-ethylhexyl) ester, sodium **salt**
CAS No.	: 577-11-7
Printing date	: 30.04.2001

1.2 SYNONYMS

1,4-Bis(2-ethylhexyl) sodium sulfosuccinate

Bis(2-ethylhexyl) sodium sulfosuccinate

Bis(2-ethylhexyl) sulfosuccinate sodium

Di(2-ethylhexyl) sulfosuccinate sodium

Di(2-ethylhexyl) sulfosuccinic acid, sodium salt

Di-2-ethylhexyl sodium sulfosuccinate

Dioctyl sodium sulfosuccinate

Dioctyl sulfosuccinate sodium

Docusate sodique

Docusate sodium

Docusatnatrium

Sodium docusate

Sodium dioctyl sulfosuccinate

Sodium dioctyl sulphosuccinate

Succinic acid, sulfo-,1 ,4-bis(2-ethylhexyl) ester, sodium salt

Sulfobutanedioic acid 1,4-bis(2-ethylhexyl)ester sodium salt

2.1 MELTING POINT

Value	ca. 162.5 - 168.5" C
Method	other:calculated
Year	2000
GLP	not applicable for estimations
Test substance	bis(2-ethylhexyl) sodium sulfosuccinate
Remark	The melting point is estimated by the EPIWIN/MPBPWIN model, using Joback, and Gold and Ogle methods.
Reliability	(2) valid with restrictions. Data were obtained by modeling.

05.03.2001

2.2 BOILING POINT

Value	ca. 483" C at 750 mm Hg
Decomposition	**yes**
Method	other: calculated
Year	2000
GLP	not applicable for estimations
Test substance	bis (2-ethylhexyl) sodium sulfosuccinate
Remark	The boiling point is estimated using EPIWIN/Stein and Brown Method. In actuality the substance, as a salt, is expected to decompose at elevated temperatures before boiling.
Reliability	(3) invalid. The material will decompose before boiling.

05.03.2001

2.4 VAPOUR PRESSURE

Value	<.00001 hPa @ 25
Method	other (calculated)
Year	**1990**
GLP	no data
Test substance	bis(2-ethylhexyl) sodium sulfosuccinate
Reliability	(2) valid with restrictions. Documentation as to how value was obtained is missing.

05.03.2001 (19)

2.5 PARTITION COEFFICIENT

Log Pow	ca. 6.1 at 25" C
Method	other (calculated)
Year	2000
GLP	not applicable for estimations
Test substance	bis (2-ethylhexyl) sodium sulfosuccinate
Remark	The log Kow was estimated using EPIWIN/KOWWIN based on molecular structure and functionality.
Reliability	(2) valid with restrictions. Data were obtained by modeling.

05.03.2001

2.6.1 WATER SOLUBILITY

Value	: ca. .00123 g/l at 25" C
PH	= 7
Method	: other: calculated
Year	: 2000
GLP	: not applicable for estimations
Test substance	: bis(2-ethylhexyl) sodium sulfosuccinate
Remark	: The value of .001227 mg/l is estimated by the EPIWIN/WSKOW model based on log Kow. This result conflicts with measured values.
Reliability	: (2) valid with restrictions. Data were obtained by modeling.

0503.2001

Value	: 15 g/l at 25" C, 23 g/l at 40" C, 30 g/l at 50" C, 55 g/l at 70" C
Method	: no data
Year	: 1983
GLP	: no data
Test substance	: bis(2-ethylhexyl) sodium sulfosuccinate
Remark	: This result conflicts with EPIWIN estimation.
Reliability	: (2) valid with restrictions. Details on experimental conditions are not present.

05.03.2001 (28)

3.1.1 PHOTODEGRADATION

Type	: air
Light source	: other
Rel. intensity	based on Intensity of Sunlight
Conc. of subst.	: at 25" C
Direct photolysis	
Halflife t1/2	: = 5.6 hour(s)
Method	: other: calculated
Year	: 2000
GLP	: not applicable for estimations
Test substance	: bis(2-ethylhexyl) sodium sulfosuccinate
Remark	: A rate constant at 25" was estimated using the Atmospheric Oxidation Program (AOPWIN) that estimates the rate constant for the atmospheric gas-phase reaction between photochemically produced hydroxyl radicals and ozone with organic chemicals. The estimated rate constant was then used to calculate the atmospheric half-life based upon the average atmospheric concentration of hydroxyl radicals.
Result	: EPIWIN estimates a hydroxyl radical rate constant of 23.05 E-12 cm^3/molecule-sec.
Reliability	: (2) valid with restrictions. Data were obtained by modeling.
05.03.2001	

3.1.2 STABILITY IN WATER

Type	: abiotic
t1/2 pH7	: ca. 6.7 year at 25" C
t1/2 pH 8	: ca. 243 day at 25° C
Method	: other: calculated
Year	: 2000
GLP	: not applicable for estimations
Test substance	: bis(2-ethylhexyl) sodium sulfosuccinate
Remark	: Stability values were estimated by the EPIWIN/HYDROWIN model based on molecular structure and functionality.
Reliability	: (2) valid with restrictions. Data were obtained by modeling.
05.03.2001	

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	: volatility
Media	: water – air
Air (level III)	: .29
Water (level III)	: 15.5
Soil (level III)	: 84.2
Method	: other: calculated
Year	: 2000
GLP	: not applicable for estimations
Test substance	: bis(2-ethylhexyl) sodium sulfosuccinate
Remark	: Level III Fugacity was estimated using the Mackay model (the currently

accepted model for estimation of theoretical distribution) with standard defaults. The 84.2% estimated for soil consists of 46.8% to soil and 37.4% to sediment.

Result : The EPIWIN model estimates a Henry's Law Constant of 5.00E-12 atm-m^3/mole. The EPIWIN model estimates a **Koc** of 1040.

Reliability : (2) valid with restrictions. Data were obtained by modeling.
05.03.2001

3.5 BIODEGRADATION

Type : aerobic
Inoculum activated sludge
Contact time : 28 day
Degradation : = 66.4% after 28 day
Result : not readily biodegradable
Kinetic of test substance : 5day 0 %
15 day 42.8 %
28 day 66.4 %
Control substance : aniline
Kinetic : 5day 18.5 %
15 day 66.7 %
28 day 98.1 %
Method OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
Year : 1991
GLP : yes
Test substance other TS

Result : The sample stock solution fell within the organic content range stated in the formula. The sample containing 1 mg/l degraded by 0%, 40.7% and 77.8% over 5, 15 and 28 days, respectively. The sample containing 2 mg/l degraded by 0%, 38.9% and 66.7% over 5, 15 and 28 days, respectively. The sample containing 5 mg/l degraded by 0%, 48.9% and 54.8% over 5, 15 and 28 days, respectively. The average degradation for the three concentrations was 0%, 42.8% and 66.4% over 5, 15 and 28 days, respectively. Aniline degraded by 18.5, 66.7 and 98.1% over the three time periods. Because a level of 70% was not reached, the test substance is not "Readily Biodegradable" by this test procedure.

Test condition : Stock solution was prepared by adding 1 g of sample to 1 liter of distilled water. The stock solution was screened to determine if it had a similar percent carbon content as stated in the formula provided by the supplier. Stock solution was diluted to 100 ppm as carbon after analysis. The diluted stock was then added to BOD bottles at 3.33 ml, 6.67 ml and 16.65 ml to yield test concentrations of 1 mg, 2 mg and 5 mg as carbon, respectively. Test solutions were inoculated with a low concentration of microorganisms from a mixed population and kept in closed bottles in the dark at a constant temperature of 20 ± 1° C. The activated sludge bacteria was from Bergen Co., New Jersey. The degradation was followed by oxygen analyses with the YSI Dissolved Oxygen Analyzer 54A over a 28-day period. Degradability was based on a comparison of readings of actual oxygen demand to the theoretically expected oxygen demand. A parallel control with inoculum, but without test material, was run as a blank correction factor. The procedure was validated by means of a reference substance (aniline, 2 mg/l) of known biodegradability.

Test Substance : $C_2OH_{37}0_7NaS$ (>97%), H_2O (< 2%), C_8H_{18} (< 1%), $C_2OH_{36}O_4$ (<0.5%), $H_2O_4S.2Na$ (<0.5%), $H_2O_3S.2Na$ (~0.2%). Carbon content was 53.5%.

Reliability : (1) valid without restriction
30.01.2001

(26)

Type	: aerobic
Inoculum	: other:predominantly gram negative bacteria
Concentration	: 1.25mmol/l
Contact time	: 4 hour(s)
Result	: other:biodegradable
Method	: other
Year	: 1999
GLP	: no data
Test **substance**	: other TS

Result : A biodegradation rate of 31.3 micromoles surfactant/min.g cell protein was calculated for bis(2-ethylhexyl) sodium sulfosuccinate

Test condition : The bacterial consortium was obtained from a detergent-polluted soil by enrichment cultivation and adaptation in the presence of surfactant 9 (mono-n-dodecyl sulfosuccinate). Bacteria were cultivated under aeration at 25" C in a phosphate mineral medium. Surfactant 9 was added to the culture in a crystalline form to a final concentration of 0.5 g/l. Microscopic examination of microorganisms present in the adapted mixed culture revealed predominantly Gram-negative motile bacteria. The rate constants of primary biodegradation of IO different alkyl sulfosuccinates (including bis(2-ethylhexyl) sodium sulfosuccinate) at a concentration of 1.25 mmol/l by the adapted mixed culture (cell protein 0.4 g/l) were measured at 25" C over 4 hours. The culture was incubated under stirring and samples were taken (times not noted) to determine the amount of surfactant remaining. The extent of biodegradation was estimated as a loss of methylene blue active substances in a chloroform extract of the media. The rate constants were calculated as maximum rates of primary degradation catalyzed by one gram of biomass protein in the initial phase of the reaction.

Test Substance : The test substance was listed as bis(2-ethylhexyl) sulfosuccinate from Sigma. As Sigma markets this chemical as the sodium salt, it is likely that the sodium salt was used in this study.

Reliability : (1) valid without restriction
27.02.2001

(27)

3.7 BIOACCUMULATION

BCF	: **ca. 56.2** at 25" C
Method	: other: calculated
Year	: 2000
GLP	: not applicable for estimations
Test substance	: bis(2-ethylhexyl) sodium sulfosuccinate

Remark : The BCF was estimated using EPIWIN/BCF program based on log Kow.

Reliability : (2) valid with restrictions. Data were obtained by modeling.
05.03.2001

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	: static
Species	: Lepomis sp.
Exposure period	: 96 hour(s)
Unit	: mg/l
Analytical monitoring	: no data
NOEC	: m = 32
LC50	: c = 37
Method	: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year	: 1987
GLP	: yes
Test substance	: bis(2-ethylhexyl) sodium sulfosuccinate

Remark : Using the Acute-Toxicity Rating Scale, published by the U.S. Fish and Wildlife Service, this substance is slightly toxic to bluegill sunfish

Result : Temperature remained steady throughout the experiment. The pH decreased from 7.6 to 7.1-7.2 by 48 hours. Dissolved oxygen decreased from approximately 8.3 to 6.1-6.5 mg/l by 48 hours, and to 5.9- 6.2 mg/l (70% saturation) by 96 hours. All solutions had a small amount of undissolved compound at 0 hours, which increased slightly with increasing concentration. A small amount of undissolved material was present in chambers containing 56, 75 and 100 mg/l after 24 hours. Chambers containing 42 mg/l were slightly cloudy at 48 and 72 hours. None of the controls or fish exposed to 32 mg/l died. There was 100% mortality by 96 hours in fish exposed to 42 mg/l and by 24 hours in those exposed to 56, 75 or 100 mg/l. The 96-hour LC_{50} was 37 mg/l. The NOEC was 32 mg/l, based on the lack of mortality and abnormal effects.

Test condition : A 96-hour static bioassay was conducted on Bluegill Sunfish (average weight 0.27 +/- 0.16 g, average length 22 +/- 3.7 mm). All fish were acclimated for at least 14 hours prior to testing. Fish were fed with commercial fish food occasionally supplemented with brine shrimp daily until 48-96 hours prior to testing. Ten fish were exposed per group to 0 (control), 32, 42, 56, 75, or 100 mg/l test material. Test material purity was specified as 99+% in the protocol. Tests were conducted in 5 gallon vessels containing 15 liters of soft, reconstituted water (total hardness of 4-48 mg/l as $CaCO_3$, total alkalinity of 25-35 mg/l as $CaCO_3$ and initial pH of 7.2 to 7.6) at 22 +/- 1 ° C. Water quality parameters of temperature, dissolved oxygen, and pH were measured throughout the test. Initial dissolved oxygen and pH were 8.3 mg/l and 7.6, respectively. Tanks were not aerated during the tests.

Data were analyzed according to a computerized LC50 program, which utilized the binomial, moving average and probit tests.

Reliability : (2) valid with restrictions. High concentrations of test material may have been insoluble.

27.02.2001 (3)

Type	: static
Species	: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period	: 96 hour(s)
Unit	: mg/l
Analytical monitoring	: no data
NOEC	: m = 20
LC50	: c = 28
Method	: Other:APHA

Year : **1985**
GLP : no data
Test substance : sodium docusate

Result : The initial dissolved oxygen and pH of the tanks ranged from 9.8-9.9 ppm and 7.84- 7.97, respectively. At 48 hr, initial dissolved oxygen and pH of the tanks ranged from 9.6-9.8 ppm and 7.69 to 7.76, respectively. Temperature at 48 hours was 11.9 to 12.0" C. Water quality parameters at 96 hours were not listed. None of the controls or fish exposed to 10 or 20 ppm died within 96 hours. All fish exposed to 40 or 80 ppm died within 24 hours. The LC50 was evaluated using probit methods, moving average angle, and Trinned Spearman-Karber. The values were 27.1, 28.3, and 28.3, respectively.

Test condition : Rainbow trout fingerlings (average weight 4.8 g) were acclimated (time not noted) in flowing dechlorinated Milwaukee tap water at 12" C. Fish were fed a commercially prepared pelleted feed during acclimation. Tests were performed in 5 gallon aquariums. Each aquarium was filled with 16 liters of dechlorinated Milwaukee tap water (12" C) and supplied with pressurized air via glass pipettes. Sodium docusate was added to 4 of the 5 aquariums used, producing concentrations of 10, 20, 40 and 80 mg/liter. Ten trout were added to each aquarium. They were not fed during the test.

Fish were observed for behavior and death every 24 hours, for a total of 96 hours. Temperature and dissolved O_2 were measured at each observation, and the pH was measured at the onset, midpoint and end of the test. Test water was replaced 48 hours into the test.

Reliability : (1) valid without restriction
30.01.2001 (7, 9)

Type : static
Species : Oncorhynchus mykiss (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
Analytical monitoring : no data
NOEC : m = 12.5
LC50 : c = 28
Method : OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year : 1990
GLP : **yes**
Test substance : bis(2-ethylhexyl) sodium sulfosuccinate

Remark : Using the Acute-Toxicity Rating Scale published by the U.S. Fish and Wildlife Service, this substance is slightly toxic to rainbow trout

Result : Temperature was maintained at 15" C throughout the test. The pH ranged from 6.8 to 7.4, and did not vary significantly according to group or time. Dissolved oxygen remained close to 9.8 mg/l in the control group and decreased to a value of 8.0 mg/l at 48 hours in the other groups. None of the controls or fish exposed to 6.25 or 12.5 ppm died. Twenty percent of fish exposed to 25 ppm died. All fish exposed to 50 or 100 ppm died within 1 hour. The NOEC was 12.5 ppm based on the lack of mortality and abnormal effects.

Test condition : This 96-hour static, non-renewal bioassay was performed on six groups of 10 Onchorhyncus mykiss (rainbow trout) approximately 70 days old. Trout were housed (5 per tank) in 4L polypropylene vessels containing 3 L of US EPA moderately hard reconstituted water. The test concentrations were 0 (control), 6.25, 12.5, 25, 50 and 100 ppm. Fish were maintained at 15 ± 2 ° C under a 16hr/8hr light/dark cycle and were not fed during tests. Oil-free air was supplied at less than or equal to 100 bubbles per minute to

maintain equal to or greater than 60% saturation. Mortality, behavior, physiology, dissolved oxygen, pH, and conductivity were measured initially and daily thereafter. Initial alkalinity and hardness of diluent were also determined. The test was considered valid if greater than 90% of control fish survived 96 hours.

Data were analyzed according to the Spearman-Karber method, Probit analysis, or graphical interpolation (where applicable).

Reliability : (2) valid without restriction
30.01.2001

(25)

4.2 **ACUTE TOXICITY TO AQUATIC INVERTEBRATES**

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
Analytical monitoring : no data
NOEC : m = 10
LC50 : c = 36.2
Method : other
Year : 1985
GLP : no data
Test substance : sodium docusate

Result : The average pH and alkalinity values obtained at 0 and 48 hours ranged from 8.42 - 8.47 and 122.1-128.7. Alkalinity increased slightly with increasing concentration. The mean temperature was 20.0 +/- 0.5" C. None of the controls or animals exposed to 5 or 10 ppm died or were found at the bottom of the test vessel. Mortality at 24 hours of those exposed to 20, 40 or 80 ppm was 0, 50, and 90%, respectively. Mortality at 48 hours of those exposed to 20, 40 or 80 ppm was 5, 60, and 1 00%, respectively. The 48- hour LC50 was evaluated using Spearman Karber, log-probit, and MAA methods. The corresponding LC50 values at 48 hours were 36.0, 36.8, and 35.8 ppm, respectively. The 48-hour NOEC was 10 ppm.

Test condition : Adult Daphnia magna were cultured in a medium containing reconstituted fresh water, Selenastrum capricornutum and trout food suspension. A stock solution was prepared prior to the bioassay at a concentration of 1 mg dioctyl sodium sulfosuccinate (DSS) per ml of solution in reconstituted water. Offspring of the adults were used in the test. Twenty animals per group were exposed to 0 (control), 5, 10, 20, 40 or 80 ppm. Animals were twenty-four hours of age or less. There were four beakers per test group and five Daphnia per test vessel (100 ml). The vessels were filled with 80 ml test water prior to introduction of Daphnia. Daphnia were not fed during the test. The test beakers were placed in constant flow water bath at 20 ± 2 °C and were covered with glass to reduce evaporation. A photoperiod of 16 hours and a light intensity of 80 foot candles was used. Temperature was measured daily and the pH and alkalinity of the test media were measured prior to and at study termination. Test animals were observed for mortality and abnormal orientation after 24 and 48 hours of exposure.

Reliability : (2) valid with restrictions. Oxygen content is unknown.
30.01.2001

(8)

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

Species	other:Tradescantia bicolor
Endpdoint	necrosis
Exposure period	48 hour(s)
Unit	mmol/l
NOEC	< 0.3125
Method	other
Year	1999
GLP	no data
Test substance	other TS

Result : At 24 hours, the necrosis scores for 0.3125 and 0.625 mmol/l were 0. The score for 1.25 mmol/l was 1. Higher concentrations induced scores of 2. At 48 hours, 0.3125 and 0.625 mmol/l induced scores of 1. Higher concentrations produced scores of 2.

Test condition : Eleven different sulfosuccinate esters were tested. Solutions of the bis(2-ethyl-hexyl) ester of sulfosuccinic acid were tested at 0.3125, 0.625, 1.25, 2.5, 5, 10 and 20 mmol/l. Test solutions were infiltrated into leaf sheets of Tradescantia bicolor plants (approximately an area of 10 x 10 mm). Distilled water was used as a control. Each experiment was run in triplicate. Phytotoxicity was evaluated after 24- and 48- hours and was scored according to the following method (0 = no effect, 1 = no necrosis but infiltrated area appears yellow, 2 = necrosis). A spectral mapping technique was used to analyze the effects of the ester compared to the other esters tested.

Test substance : The test substance was listed as the di-(2-ethyl-hexyl) ester of sulfosuccinic acid. Other studies performed by the authors list the supplier as Sigma. As Sigma markets this chemical as the sodium salt, it is likely that the sodium salt was used in this study.

Reliability : (1) valid without restriction
03.03.2001

(23)

5.1.1 ACUTE ORAL TOXICITY

Type	: LD50
Species	: mouse
Strain	: other: ARS/ICR
Sex	: male
Number of animals	: 80
Value	: = 2643 mglkg bw
Method	: other
Year	: 1977
GLP	: pre-GLP
Test substance	: dioctyl sodium sulfosuccinate

Result : Mortality rates for exposure to 2340, 2520, 2690, 2880, 3090, 3310, 3550 or 3825 mglkg were 3110, 6110, 4/10, 7110, 5110, 7110, 7110, 9110, respectively. High lethal doses caused mice to be hypoactive. Deaths at high doses occurred within 4-8 hours of dosing. The LD50 was 2643 (2029-3440) mglkg.

Test condition : Mice (IO/group) weighing 18-22 g were given 2.5 to 5.0 ml/100 g dioctyl sodium sulfosuccinate (DSS) in 4% acacia by gastric intubation. The doses administered were: 2340, 2520, 2690, 2880, 3090, 3310, 3550, and 3825 mg/kg. Mice were observed for abnormal signs and mortality for 14 days following dosing. The method of Litchfield and Wilcoxon (J Pharm Exp Ther 96:99, 1949) was used to calculate LD50 values.

Reliability : (1) valid without restriction
27.02.2001 (5)

Type	: LD50
Species	: rat
Strain	: CF Nelson
Sex	: male
Number of animals	: 20
Vehicle	: water
Value	: = 3080 mg/kg bw
Method	: other
Year	: ***1966***
GLP	: pre-GLP
Test substance	: dioctyl sodium sulfosuccinate, 100%

Result : None of the animals administered 0.625 or 1.25 g/kg died. Mortalities of rats given 2.5 or 5 g/kg were 115 and 5/5, respectively. All deaths occurred within 24 hours. Signs of intoxication included depression of varying intensity and diarrhea. No visible lesions were noted in the surviving animals at terminal necropsy.

Test condition : Four groups of 5 male rats (average weight 131 g) fasted for 24 hours were dosed with a 5% aqueous dispersion at 0.625, 1.25, 2.5, and 5.0 g/kg. At 5 g/kg, the dose was administered in 2 separate portions ¼ hour apart. Animals were observed over a period of 4 days.

Reliability : (1) valid without restriction
30.01.2001 (1)

Type	: LD50
Species	: rat
Strain	: Sprague-Dawley
Sex	: male

Number of animals	**: 20**
Vehicle	: water
Value	: = 4200 mglkg bw
Method	: other
Year	**:** 1977
GLP	: pre-GLP
Test substance	: sodium dioctyl sulfosuccinate
Remark	: LD50 listed in report was 4.2 ml/kg. This is obviously incorrect,
Result	: Mortalities of rats exposed to 14.1, 17.8, 22.4, 25.2 ml/kg (2.82, 3.56, 4.48, and 5.04 g/kg) were 0/5, 1/5, 3/5, and 5/5, respectively. Most deaths occurred within 6-24 hours of dosing. Signs of intoxication included prostration and lethargy. Yellow fluid was observed in the gastrointestinal tract of those found dead. No visible lesions were observed in the surviving animals at terminal necropsy.
Test condition	: Rats (5 per group, average weight 145-152 g) that had been fasted overnight were dosed with a 20% aqueous solution of the test material in dosages of 14.1, 17.8, 22.4 and 25.2 ml/kg (2.82, 3.56, 4.48, and 5.04 g/kg) by oral gavage. Animals were observed up to 14 days following dosing.
Reliability	: (2) valid with restrictions. Documentation as to how doses were prepared is not present.

27.02.2001 (16)

Type	: LD50
Species	: rat
Strain	: Wistar
Sex	: female
Value	**: ca. 2000** mglkg bw
Method	: other
Year	**:** 1962
GLP	: pre-GLP
Test substance	: dioctyl sodium sulfosuccinate
Remark	: The actual doses given and the number of deaths at each dose were not listed. The LD50 was listed at approximately 2 g/kg, with a range of approximately 0.8 g/kg.
Test condition	: Groups of 5 unfasted female rats (135-189 g) were given dioctyl sodium sulfosuccinate (DSS) as a 10% aqueous solution or emulsion in doses ranging in geometric progression from 0.252 to 7.95 g/kg. Mortality was monitored 2 weeks postdosing. LD50 values were calculated by the Weil Modification of the Method of Thompson.
Reliability	: (2) valid with restrictions. Number of deaths at each dose is not listed.

27.02.2001 (22)

Type	: LD50
Species	: mouse
Strain	: other:Harlan
Sex	: male/female
Value	: = 4800 mglkg bw
Method	: other
Year	**:** 1949
GLP	: pre-GLP
Test substance	: sodium dioctyl sulfosuccinate
Remark	: The doses that were given and the number of deaths at each dose were not listed.

Test condition : Mice (14-23 g) were given test material so that 0.5 cc of solution was given by gavage for each 20 g of mouse. Groups (5/sex/dose) were given test material with increasing increments between doses of 20% or less. Mice were observed over a 72-hour period. The LD50 was calculated from the death rate at the dosages given.

Reliability : (2) valid with restrictions. Doses given and number of deaths at each dose is not listed.

27.02.2001 (15)

5.1.3 ACUTE DERMAL TOXICITY

Type : **LD50**
Species : rabbit
Strain : New Zealand White
Sex : male
Number of animals : **5**
Value : > 10 g/kg bw
Method : other
Year : 1977
GLP : pre-GLP
Test substance : sodium dioctyl sulfosuccinate

Result : None of the animals died. Skin irritation including fissuring, desquamation, and coriaceousness was noted. Rabbits were noted pulling fur out. No gross pathology was observed.

Test condition : 5 male rabbits (avg. weight 2.29 kg) received a 10ml/kg dose by covered dermal application to clipped unabraded skin for 24 hours. Animals were observed over 14 days.

Reliability : (1) valid without restriction
30.01.2001 (16)

5.4 REPEATED DOSE TOXICITY

Species : rat
Sex : male/female
Strain : other:Charles River albino
Route of admin. : oral feed
Exposure period : 90 days
Doses : 1.0%
Control group : **yes**
NOAEL : >= 1 %
Method : other
Year : 1969
GLP : pre-GLP
Test substance : other TS

Result : No deaths or abnormal behavioral reactions were noted. There was no effect of treatment on final body weights, food consumption, hematologies, urinalyses, organ weights, or gross or microscopic pathology (as compared to controls).

Test condition : Design: 20 albino rats / sex were fed test material for 90 days at a dietary concentration of 1 .0%, which was prepared by blending the appropriate

amount of test material with standard rat ration. Twenty control rats/sex received normal food. Rats were weighed biweekly, and food consumption was recorded weekly. Fresh diets were prepared weekly. Standard hematologies and urinalyses were performed on blood and urine samples collected from 5 rats/sex/group on treatment day 84.

Endpoints: Animals were sacrificed 90 days after treatment and a complete set of organs and other tissues was examined. At autopsy, the weight of the liver and kidneys of 10 rats/sex/group were recorded. The following tissues from 5 rats/sex/group were examined histologically: esophagus, stomach (cardia, fundus, pyloris), small intestine (duodenum, jejunum, ileum), cecum, colon, liver, kidneys, spleen, pancreas, urinary bladder, pituitary, adrenal, testes, seminal vesicle, ovary, bone marrow, thyroid, parathyroid, salivary gland, prostate, heart, aorta, lung, lymph node (cervical and mesenteric), skeletal muscle, peripheral nerve, bone (femur), spinal cord, uterus, trachea, eye, optic nerve and brain (cerebrum, cerebellum, and pons).

Statistical Analyses: Data for food consumption, weight, absolute organ weights and organ/body weight ratios were analyzed by analysis of variance (ANOVA). Effects uncovered were further analyzed by t-tests.

Test substance

A commercial sample of CAS 577-l l-7 was dried to remove the liquid phase. The dried products were 100% solids or "active ingredients"

Reliability
02.03.2001

(1) valid without restriction

(17)

Species	dog
Sex	male/female
Strain	Beagle
Route of admin.	other: oral tablet
Exposure period	1 year
Frequency of treatment	once per day, 7 dlwk
NOAEL	>= 30 mglkg
Method	other
Year	1977
GLP	pre-GLP
Test substance	dioctyl sodium sulfosuccinate

Result

There were no effects of treatment with DSS on organ or body weights, gross and microscopic tissue observations, or hematological, blood chemistry, or urinalysis parameters. No evidence of gastric irritation was noted

Test condition

72 dogs (7-8 months of age) were conditioned for approximately 6 weeks prior to compound administration. They were divided into 9 groups of 8 dogs each (4 of each sex). Groups of dogs were dosed orally with tablets containing danthron (5 or 15 mglkg), dioctyl sodium sulfosuccinate (DSS; 30 mglkg), poloxalkol (POL; 120 mglkg), danthron (5 or 15 mg/kg) + DSS (10 or 30 mg/kg), or danthron (5 or 15 mglkg) + POL (40 or 120 mglkg) once a day, seven days/week, for one year. A control group received a daily quantity of tables that contained all materials in the 15 mg danthron tablets except the active material. All formulations met appropriate analytical specifications. All dogs were weighed at weekly intervals and doses were adjusted accordingly. Physical examinations were conducted pre-dose and at 3, 6, 9 and 12 months post dose. Urinalyses were done on urine samples collected pre-dose and at 6 and 12 months. Standard hematology parameters and serum chemistries were determined on blood collected from the external jugular vein on days -28, -7, 14, 30, 80, 130,

210, 280, and 365. Fundus photographs were taken pre-dose and just prior to termination. Various tissues were weighed and examined microscopically at termination.

Reliability : (1) valid without restriction
27.02.2001 (5)

Species : rat
Sex : male
Strain : Osborne-Mendel
Route of admin. : oral feed
Exposure period : 16 weeks
Doses : 2, 4, 8 %
Control group : **yes**
NOAEL : < 2 %
LOAEL : = 2 %
Method : other
Year : 1948
GLP : pre-GLP
Test substance : dioctyl sodium sulfosuccinate

Result : All animals that received 8% had severe GI symptoms and died within the first week of treatment. Only one animal given 4% lived for 16 weeks and it grew slowly. Rats given 2% gained less weight than controls (220.4 +/- 24.9 g vs. 393.0 +/- 22.6 g) and had evidence of gastrointestinal irritation upon necropsy

Test condition : Groups of 5 male rats (21 days old) received diet (ground commercial rat biscuits) containing 2, 4, or 8% dioctyl sodium sulfosuccinate (DSS) or a control diet containing 1% cod liver oil. Test material was mixed with the diet by means of a rotary batch mixer. Body weights and food consumption were determined at weekly intervals. Surviving animals were sacrificed and subjected to necropsy after 16 weeks. Lung, heart, liver, spleen, pancreas, stomach, small intestine, kidney, adrenal and testes were sectioned in all instances and colon, thyroid, parathyroid, lymph nodes, leg bones, leg muscles, and bone marrow were sectioned in some (number not noted).

Reliability : (2) valid with restrictions. Whether fresh diets were prepared frequently is not documented. It is assumed that the test diet was only prepared at the beginning of the experiment.
27.02.2001 (6)

Species : rat
Sex : male/female
Route of admin. : oral feed
Exposure period : 26 weeks
Doses : 0.5, 1.04, 1.5%
Control group : yes, concurrent no treatment
NOAEL : = .5 %
LOAEL : = 1.04 %
Method : other
Year : 1966
GLP : pre-GLP
Test substance : dioctyl sodium sulfosuccinate

Result : Weight gain of females given 1.04 or 1.5% was reduced during the third week. Two controls and 4 test animals given 1.5% died. Two out of the four that died after 1.5% exhibited hemorrhagic gastroenteritis. No other effects were noted.

Test condition : Groups of 12 male and female weanling rats were treated with diets containing 0. 0.5, 1.04 and 1.5% dioctyl sodium sulfosuccinate (DSS) for 26 weeks. Body weight and food consumption were monitored over the course of the study. Hematological analysis and urinalyses were performed. The weight of the spleen, liver, adrenal, kidney and gonads was determined at autopsy. Heart, lung, liver, spleen, kidney, adrenal, bladder, thyroid, pancreas, lymph nodes, gut, muscle, bone, marrow, gonads and thymus were examined histologically.

Reliability : (2) valid with restrictions. The primary reference was not available.
27.02.2001

(24)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test
System of testing : Salmonella strains TA98, TAIOO, TA1 535, TA1 537 and TA1 538
Concentration : 0, 1, 10, 100 micrograms/plate
Metabolic activation : with and without
Result : negative
Method : other
Year : 1980
GLP : no data
Test substance : dioctyl sodium sulfosuccinate

Result : Tests with all strains were negative at all concentrations. Results for two strains (TA98 and TAIOO) were listed. The number of revertants in TA98 incubated with 0, 1, 10 or 100 micrograms without metabolic activation were 22, 31, 32 and 35, respectively, and with metabolic activation were 58, 50, 43, and 55, respectively. The number of revertants in TAIOO incubated with 0, 1, 10 or 100 micrograms without metabolic activation were 201, 183, 180 and 185, respectively, and with metabolic activation were 158, 146, 135, and 140, respectively.

Test condition : Salmonella strains TA98, TAIOO, TA1535, TA1537 and TA1538 were cultured according to established procedures. Liver microsomes were prepared from Sprague-Dawley rats 5 days after a single i.p. injection of 500 mg/kg Aroclor 1254. The livers of animals were homogenized, pooled and centrifuged at 9000 g for 10 min and the resulting supernatant (S-9) was stored at -90° C until required. S-9 mix was prepared with NADP, MgCl2, KCl and glucose-6-phosphate as cofactors.

Concentrations of test materials (dioctyl sodium sulfosuccinate and 23 other food additives) ranging from 100 micrograms to 10 mg per plate were first tested for cytotoxicity. For each Salmonella strain, duplicate plates were set up with 4 dilutions of test materials in dimethyl sulfoxide in the optimal non-toxic dose range with or without S-9 mix. Bacteria from an overnight stationary-broth culture (1 0E*8 organisms/ml), test material, and S-9 mix (as required) were mixed in 2 ml of minimal agar at 42" C. This was added to 30 ml of minimal agar in 100 mm Petri plates and incubated at 37° C for 48 hours. The number of His+ revertant colonies was then enumerated.

Reliability : (2) valid with restrictions. There was no positive control.
27.02.2001

(4)

Type : Ames test
System of testing : Salmonella strains TA98, TA1 00, TA102, TA1535 and TA1 537
Concentration : micrograms/plate
Metabolic activation : with and without

Result : negative
Method : OECD Test guideline 471
Year : 1993
GLP : **yes**
Test substance : sodium dioctyl sulphosuccinate

Result : Cytoxicity (as evidenced by the thinning of the background bacterial lawn) was observed at the highest concentration used in experiments 1 and 2 and the top two concentrations used in experiments 3 and 4. The test was considered valid. No concentration of sodium dioctyl sulphosuccinate, either in the presence or absence of S-9 resulted in a statistically significant increase in the number of revertants in any of the test strains.

Test condition : Salmonella strains TA98, TA100, TA102, TA1535 andTA1537. Liver S-9 that was prepared from male Sprague-Dawley rats induced with Aroclor 1254 (MolTox S-9) was obtained from Molecular Toxicology Incorporated, Anapolis MD. The S-9 was stored at -80° C until use. Each batch was tested by the manufacturer for sterility, protein content (minimum 32 mg/ml), ability to convert ethidium bromide and cyclophosphamide to bacterial mutagens, and cytochrome p-450-catalyzed enzyme activity.

Test chemical solutions were prepared by dissolving sodium dioctyl sulphosuccinate in analytical grade acetone. Test chemical solutions were protected from light and were used within 24 hours of preparation. A range-finding study was first performed to determine cytotoxic concentrations. Four separate mutagenicity experiments were performed. The concentrations used in the first experiment were 1.6, 8.0, 40, 200 and 1000 micrograms per plate. The concentrations used in the second experiment were 4, 20, 100, 50 and 2500 micrograms per plate. The third experiment used 62.5, 125, 250, 500 and 1000 micrograms per plate, and the fourth used 156.25, 312.5, 625, 1250 and 2500 micrograms per plate. S-9 was used in the second and fourth experiments. The solvent (acetone) was also tested for mutagenicity. The positive controls 2-nitrofluorene (50 micrograms per plate), sodium azide (2 micrograms per plate), 9-aminoacridine (50 micrograms per plate), glutaraldehyde (25 micrograms per plate) and 2-aminoanthracene (5 micrograms per plate) were tested in strains TA98, TA1 00 and TA1 535, TA1 537, TA1 02, and an unlisted strain, respectively. Bacteria that had been checked for strain characteristics were cultured for 10 hours at 37° C in nutrient broth. Triplicate plates containing 2.5 ml molten agar were prepared for each concentration. For experiments 2 and 4, 0.5 ml S-9 mix was added to each plate. Bacteria were added at 0.1 ml bacterial culture per plate (number of bacteria not noted) and test agent was added at 0.05 ml per plate. Plates were inverted and incubated at 37° C in the dark for 3 days. Colonies were counted electronically and inspected for signs of toxicity.

The m-statistic was calculated to check that the data were Poisson distributed. Dunnett's test was used to compare the counts at each dose to control. The presence of a dose-response was examined using linear regression. The assay was considered valid if negative controls fell within a historical range, positive controls induced clear increases in revertants, and no more than 5% of the plates were lost due to contamination or error.

Reliability : (1) valid without restriction
27.02.2001 (11)

Type : Chromosomal aberration
System of testing : Chinese Hamster Ovary (CHO) Cells
Concentration : micrograms/plate
Metabolic activation : with and without
Result : negative

Method : OECD Test guideline 471
Year : **1993**
GLP : **yes**
Test substance : sodium dioctyl sulphosuccinate

Result : The test was considered valid. Positive controls induced significant increases in the number of cells with aberrations, the proportion of cells with aberrations in negative control cultures were within normal range for all but two of the cultures, and at least 160/200 cells were analyzed at each treatment level. In experiment 1, approximately 52% and 19% mitotic inhibition was observed following treatment with 55.3 or 112.8 micrograms/ml in the absence or presence of S-9, respectively, Complete toxicity was observed at higher doses. Additional experiments were therefore conducted at dose ranges expected to induce 50-75% mitotic inhibition. Treatment of cultures with sodium dioctyl sulphosuccinate (DSS) in the absence of S-9 resulted in aberration frequencies similar to those of negative controls. Cultures treated with DSS in the presence of S-9 in Experiment 2 had significantly increased frequencies of cells with aberrations (compared to historical controls) at the highest dose chosen for analysis (120 micrograms/ml). Approximately 62% mitotic inhibition was noted at this concentration. In contrast, cultures treated with this and higher scorable concentrations (up to 130 micrograms/ ml) in other experiments had normal frequencies of aberrations. However, mitotic inhibition of at least 50% was not observed at these concentrations in these experiments. In all experiments, treatment with 140 micrograms/ml caused complete toxicity.

Test condition : Liver S-9 that was prepared from male Sprague-Dawley rats induced with Aroclor 1254 (MolTox S-9) was obtained from Molecular Toxicology Incorporated, Annapolis MD. The S-9 was stored at - 80" C until use. Each batch was tested by the manufacturer for sterility, protein content (minimum 32 mg/ml), ability to convert ethidium bromide and cyclophosphamide to bacterial mutagens, and cytochrome p-450-catalyzed enzyme activity. As needed, a 0.25 ml aliquot of S-9 was added to each cell culture (4.75 ml).

Sodium dioctyl sulfosuccinate was tested for cytogenicity using duplicate cultures of CHO cells in the presence and absence of S-9. The highest dose used (470 micrograms/ml) was close to the solubility limit in the culture medium. Stock solutions were prepared by dissolving test material in acetone to give 47 mg/ml. Stock solutions were diluted with acetone to make test concentrations ranging from 9.3 to 470 micrograms/ml for Experiment 1, 70 to 160 micrograms/ml for Experiment 2, 10 to 140 micrograms/ml for Experiment 3, 101 to 140 micrograms/ml for Experiment 4, and 90 to 170 mg/ml for Experiment 5. Acetone was also tested as a vehicle control. The positive control chemicals 4-nitroquinoline l-oxide (0.0625, 0.125, 0.25 micrograms/ml) and cyclophosphamide (12.5 and 25.0 micrograms/ml + S9) were also tested. All test solutions were used within 2.5 hours of preparation.

CHO cells of low confluence were used in the tests (number not indicated). In experiment 1, cells were incubated in the absence of S-9 for 20 hours, or in the presence of S-9 for two hours, followed by 18-hrs of recovery. In experiments 2, 3, and 5, the S-9 protocol for experiment 1 was followed. Experiment 3 followed the protocol of experiment 1 , plus additional plates were incubated for 44 hours in the absence of S-9. Cultures were prepared in duplicate or quadruplicate. Colchicine was added at 1 microgram/ml approximately 1.5 hours prior to harvest to arrest dividing cells in metaphase. Cells were harvested , fixed, stained with Giemsa, and examined for mitotic index. Twenty-five cells from each of the positive control cultures were analyzed to ensure that the test was valid. Where possible, 100 metaphases from each test and negative control culture were

analyzed for chromosome aberrations. Aberrants were categorized as 1) cells with structural aberrations including gaps, 2) cells with structural aberrations excluding gaps, and 3) polyploid, endoreduplicated or hyperdiploid cells. The proportion of cells in category 2 for each test condition was examined with the proportion in negative controls using Fisher's exact test. The proportions of cells in categories 1 and 3 were examined in relation to historical controls.

Conclusion : The fact that chromosome aberrations were observed only at a dose level close to the toxic threshold implies that DSS did not have a direct effect on DNA.

Reliability : (1) valid without restriction
27.02.2001 (12)

5.7 CARCINOGENICITY

Species : rat
Sex : male
Strain : Osborne-Mendel
Route of admin. : oral feed
Exposure period : 2 years
Doses : 0.25, 0.5, 1 .O %
Control group : **yes**
NOAEL : = .5 %
LOAEL : = 1 %
Method : other
Year : 1948
GLP : pre-GLP
Test substance : dioctyl sodium sulfosuccinate

Result : There was no effect of DSS on food intake. Consumption of 1 .O% DSS in the diet was associated with significantly less weight gain (395.8 +/- 11.6 g) than controls (471.9 +I- 13.2 g). There was no other effect of treatment on the animals.

Test condition : Groups of 12 male rats (21 days old) received diet (ground commercial rat biscuits) containing 0.25, 0.5 and 1 .O% dioctyl sodium sulfosuccinate (DSS) or a control diet containing 1% cod liver oil. Test material was mixed with the diet by means of a rotary batch mixer. Body weights and food consumption were determined at weekly intervals. Surviving animals were sacrificed and subjected to necropsy after two years. Lung, heart, liver, spleen, pancreas, stomach, small intestine, kidney, adrenal and testes were sectioned in all instances and colon, thyroid, parathyroid, lymph nodes, leg bones, leg muscles, and bone marrow were sectioned in some (number not noted).

Reliability : (2) valid with restrictions. The stability of test material in the diet and when diets were prepared is not documented.
27.02.2001 (6)

5.8 TOXICITY TO REPRODUCTION

Type : other: three generation
Species : rat
Sex : male/female
Strain : other: Crl:CD (SD)BR
Route of admin. : oral feed

Premating exposure period	
Male	IO weeks
Female	2 weeks
Doses	0.1, 0.5, 1.0%
Control group	yes
NOAEL Parental	= .1 %
NOAEL F1 Offspr.	= .1 %
NOAEL F2 Offspr.	= .1 %
Method	other
Year	1986
GLP	yes
Test substance	dioctyl sodium sulfosuccinate

Remark

The NOEL listed is for effect on lactation

Result

Dietary composition: Average concentrations of DSS in the diets were 0.0984% and 0.972% for the 0.1 and 1 .0% dose levels, respectively. DSS did not hydrolyze in the diet to form significant amounts of 2-ethylhexanol. The level of acetone in the diets (< 50 ppm and 50.2 ppm for the 0.1 and 1 .0% dose groups, respectively) was not expected to affect the results of the study.

Food consumption and body weight: Food consumption of FO, Fl and F2 males treated with 1 .0% DSS was significantly less than controls at week 4, weeks 2, 4, 8, and 10, and weeks 2 and IO, respectively. There was no consistent effect of any dose on food consumption in females. Body weights of FO, F1 and F2 males treated with 1.0% and F1 and F2 females treated with 0.5 or 1 .0% were lower than controls during the premating phase. All three generations of pups born to animals treated with 0.5% or 1 .0% weighed significantly less than controls on Day 21. No milk was found in the abdomens on lactation day 4 in 3 control F2 pups, 7 F2 pups in the 0.1% dose group, 18 F2 pups and 1 F3 pup in the 0.5% dose group, and IO F2 pups and 17 F3 pups in the 1 .0% dose groups.

Reproductive indices: There was no effect of treatment on the total and mean number of pups born alive, litter size, survivability, or sex ratio. Perinatal pup survival across the three generations was 99% for controls and ranged from 96% to 100% for the treated groups. Pup survivability ranged from 95-100% for controls, from 98-100% for low- and mid-dose groups and from 91-99% for the high dose group. There were no treatment-related mortatily and antemortem or microscopic observations in any animals examined (FO, F1 and F2 adults and F3 weanlings).

Test condition

Treatment: Test diets (ground Purina Certified Rodent Chow No. 5002) containing 0.1, 0.5 or 1 .0 dioctyl sodium sulfosuccinate (DSS) dissolved in acetone were mixed weekly. Samples of test diets were assayed periodically for DSS to verify homogeneity and stability of DSS after storage. After a 4-week acclimation period, groups of 30 male and 30 female rats (7 weeks of age, guaranteed non littermates) were fed the basal diet or a test for IO and 2 weeks, respectively. These animals (FO) were then mated to produce an F1 litter. Groups of 30 male and 30 female F1 animals were fed the same dose levels for at least IO weeks postweaning, and the breeding program was repeated to produce F2 animals. Sibling and half-sibling matings were avoided. Groups of 30 male and 30 female F1 animals were fed the same dose levels for at least IO weeks postweaning, and the breeding program was repeated to produce F2 animals. The same feeding and mating procedure was repeated with F2 animals to produce F3 offspring. The study was terminated upon weaning of the F3 generation.

Data: Individual pup weights and the number of pups born live or found

dead were recorded on lactation Day 0. Intact dead pups were examined and preserved. The number and sex of pups and individual pup weights were recorded on lactation Day 4. Pups were culled from litters to achieve a maximum of 10 (5 of each sex if possible)/ litter. Pups were weighed and examined externally on Days 7, 14 and 21 of lactation. At least one male and female/litter (for a total of 30/sex/group) were selected to continue on the study. Twenty weanlings/sex/group from the F3 litter were necropsied. Weanlings not selected for mating or necropsy were examined externally. All FO, F1 and F2 animals were observed twice daily during the study and subjected to gross necropsy upon study termination. Organs grossly examined at necropsy were colon, duodenum, epididymides, ileum, jejunum, kidneys, liver, mammary gland (with skin), ovaries, prostate, seminal vesicles, stomach, testes, uterus and vagina. Body weights were recorded weekly for males and before mating, Days 0, 7, 14 and 20 of gestation and Days 0, 7, 14 and 21 of lactation for females. Food consumption of males females was recorded weekly before mating, and twice weekly during gestation and lactation (females only).

Statistical Analyses: Body weight, food consumption, reproductive indices, precoital interval, length of gestation, pup viability and body weight, sex ratios and litter size (alive and dead by sex) were analyzed using a one-way ANOVA. When necessary, data were transformed to achieve homogeneity. Dunnett's t-test was used to compare means of groups analyzed by ANOVA. Data that could not be transformed to homogeneity were analyzed nonparametrically, using a Kruskal-Wallis test. The Nemenyi , Nemenyi-Kruskal-Wallis or Wilcoxon-Mann-Whitney two sample rank test were used compare nonparametric means. Reproductive indices and the total number of live and dead pups were analyzed by the Cochran-Armitage test for trend and the Fisher-Irwin exact test for heterogeneity.

Test substance Purity was 99.4%

Conclusion DSS at 0.5 and 1 .O% affected lactation. Reduced body weights in animals receiving 0.5 or 1 .O% did not interfere with growth and development or normal reproductive performance.

Reliability (1) valid without restriction
27.02.2001 (10, 20)

Type	other:three generation
Species	rat
Sex	male/female
Strain	other:CFE
Route of admin.	oral feed
Doses	0.5, 1.0%
Control group	yes
NOAEL Parental	< .5 %
NOAEL F1 Offspr.	< .5 %
NOAEL F2 Offspr.	< .5 %
other: NOEL F3 Offspring	< .5 %
Method	other
Year	1970
GLP	pre-GLP
Test substance	other TS

Remark Results are based on the concentration of DSS in the diet, and not the original test material. It is presumed that the test material was dried to remove ethanol.

The lowering of survival rate of the F3b pups was attributed to impairment of nutrition, presumably because of the taste of DSS secreted in the milk of

the dams. Skeletal changes were concluded to be unrelated to DSS. The NOAELs listed are for an effect on lactation,

Result : No effects of DSS on fertility and gestation indices were noted in the FO generation and F2 generation dams that were continuously fed test diet. The viability index was slightly depressed for F3b pups from dams given 0.5 or 1.0% (78 and 72 vs. 93 for controls). The lactation index for both FO and F2 dams that were fed test diet continuously at 0.5 or 1 .0% DSS was depressed (46 and 42 for versus control of 64 for Fla pups and 59 and 53 versus control of 71for F3b pups). For these groups, the mean weight of pups decreased slightly with increasing concentration of DSS in the diet of dams.

With the exception of F1b pups, no effect of DSS on lactation indices and viability index was noted in pups (F2, F3a) from dams that did not receive DSS during lactation.

Autopsy and skeletal studies of the pups indicated no significant changes, with the exception of the occasional presence of an extra sternebra in the sternum between the fifth and sixth sternebra (1/29,7/30 and 4/29 at 0. 0.5 and 1.0% DSS)

Test condition : Dioctyl sodium sulfosuccinate (DSS) was incorporated on a weight basis into rodent chow at concentrations of 0.5 and 1 .0%. Diets were prepared on a weekly basis. Test or control diets (0% DSS) were fed to groups of 40 male and female rats. Pairs of rats were mated to produce two litters per generation with the exception of the F1 b generation (which was bred once to produce a single F2 generation). The FO generation was maintained on the test diet until 3-4 months of age before mating. For the first mating of the FO and F2 generations, dams were continuously fed test diets, and the pups weaned directly onto test diets at 21 days of age. For the other 3 matings (F1 b, F2 and F3a pups), DSS was removed from the diet of the dams before they were expected to deliver, and pups were placed on test diets after weaning. Reproductive performance was assessed by determining fertility, gestation, viability and lactation indices. Litter size was reduced to 10 pups at day 5. Pups from all litters (including those that died before weaning) were examined for gross defects. Autopsies were performed on pups from the first mating of the F2 animals. Portions of all major organs from one female and one male from each litter were examined histologically. Carcasses of the other pups were cleared and skeletons were examined for defects.

Test Substance : A formulation consisting of 50% dioctyl sodium sulfosuccinate in an aqueous beverage grade ethanol solution was the original test material.

Conclusion : Lactation was affected by DSS. No effects other than those due to reduced lactation (eg. reduced lactation index, weight of pups, and survival rate) were observed. Changes in these parameters were not observed if exposure was terminated prior to lactation.

Reliability : (2) valid with restrictions. Ethanol may have been present in test material. Drying of material to remove ethanol is not documented.

27.02.2001 (2)

Type	: other: histologic examination of reproductive organs
Species	: rat
Sex	: male/female
Strain	: other:albino
Route of admin.	: oral feed
Exposure period	: 90 days
Doses	: 1 .0%
NOAEL Parental	: > 1 %

Method : other
Year : **1969**
GLP : pre-GLP
Test substance : other TS

Remark : This study was part of a 90 day oral toxicity study described in Section 5.4

Result : There was no effect of treatment on histology of any reproductive organ

Test condition : 20 albino rats / sex were fed test material for 90 days at a dietary concentration of 1 .0%, which was prepared by blending the appropriate amount of test material with standard rat ration. Weight and food consumption were monitored biweekly and weekly, respectively. Animals were sacrificed 90 days after treatment and ovaries and the uterus from females and prostate, testes and seminal vesicles from males were examined grossly and histologically.

Test substance : A commercial sample of Aerosol-OT was dried to remove the liquid phase. The dried products were 100% solids or "active ingredients".

Reliability : (1) valid without restriction
27.02.2001 (17)

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : rat
Sex : female
Strain : Sprague-Dawley
Route of admin. : oral feed
Exposure period : days 6-l 5 of gestation
Doses : 1 .0 and 2.0%
Control group : **yes**
NOAEL Teratogen : = 1 **%**
Method : other
Year : 1976
GLP : pre-GLP
Test substance : dioctyl sodium sulfosuccinate

Result : Ingestion of 1% had no effect on reproduction or condition of fetuses. The 2% dietary level produced effects that included reduced weight gain in dams, a significant increase in fetal resorptions (13.7% vs. 5.6% in controls), and a significant percentage of externally malformed fetuses (20.2% vs. 0% in controls). The abnormalities consisted primarily of exencephaly of varying degrees of severity. This malformation was frequently associated with spina bifida and microphthalmia. Skeletal observations of fetuses from rats treated with 2% showed a significant increase in incomplete ossification of various cranial bones and curved or open vertebral columns.

Test condition : Test material was prepared as a 40% solution in USP corn oil. Rats were mated when they were approximately 2 months of age. The first day following mating was counted as Day 1 of gestation. Dietary concentrations of 1 .O and 2.0% were administered to 22 and 20 female rats, respectively, on days 6-15 of gestation. Two groups of control animals received 1.5% or 2.0% corn oil in the diet. Rats were observed each day for clinical condition and signs of illness. Body weight and food consumption were recorded at various times during the test. Mothers were killed on day 21 of gestation, and fetuses were removed by cesarean section. The number of fetal implantations, resorptions, dead and viable fetuses was determined. Fetuses were grossly examined, weighed, and measured. One half of the fetuses were examined for visceral

abnormalities, and the other for skeletal abnormalities.

Maternal body weight gains, food consumption and weights were analyzed by Dunnett's two-sided, multiple comparison test. Frequencies of resorptions and abnormalities were analyzed by the Mann-Whitney U or the Chi-square test, as appropriate,

Reliability : (1) valid without restriction
30.01.2001 (13)

Species : rat
Sex : female
Strain : Sprague-Dawley
Route of admin. : oral feed
Exposure period : days 6-l 6 of gestation

Doses : **2%**
Control group : **yes**
NOAEL Maternalt. : **< 2 %**
NOAEL Teratogen : **< 2 %**
Method : other
Year : 1979
GLP : no data
Test substance : other TS

Remark : The primary reference (Hoechst-Roussel, 1979) was not available.

Result : There was a significant decrease in maternal weight, food consumption and weight gain in dams treated with 2% DSS. Following treatment with control diet, there was a compensatory weight gain among DSS treated animals, so that at term maternal weights of treated animals were similar to controls. There was no effect of treatment on reproduction. Fetuses had decreased weight and crown-rump length. Increased incidences of skeletal abnormalities were observed in the fetuses. The major skeletal abnormality observed was an increase in unossified 5th sternebrae and xiphisternum.

Test **condition** : Rats were treated with 2% corn oil in the diet (controls) or 2% dioctyl sodium sulfosuccinates on days 6-16 of gestation, and control diet thereafter.

Reliability : (2) valid with restrictions. The primary reference was not consulted.
27.02.2001 (14, 21)

5.11 EXPERIENCE WITH HUMAN EXPOSURE

Remark : Although the rate of congenital disorders in the general population was not noted, the authors concluded that there was not a strong association between docusate sodium use and congenital defects in offspring

Result : Out of the 6,837 women studied, 473 received docusate sodium during the first trimester. One infant that had been exposed to docusate sodium during this period had a congenital disorder. The estimated prevalence of a disorder in infants of women taking docusate sodium is 2/1 000, which was lower than the overall rate in the entire group (12/1000).

Test condition : Records from all liveborn infants born from July 1, 1977 to Dec 31, 1979 to mothers that were members of the Group Health Cooperative of Puget Sound for at least 280 days before delivery were analyzed. Infants with

major disorders diagnosed at birth were identified. Disorders diagnosed subsequent to the hospital admission for childbirth (such as pyloric stenosis) were excluded. Some disorders diagnosed at birth (e.g. benign skin conditions, hernia, or functional or positional disorders) were not considered. Clinical records of infants with disorders (excepting those with Down's syndrome, trisomy 18, undescended testicle, cleft lip and/or palate, or rectal atresia) were reviewed to confirm diagnoses. Infants with abnormalities noted at birth that were not confirmed upon follow-up examination were classified as not having disorders. Infants that had minor changes (e.g. syndactly of the second and third toes (n = l), polydactyly of the postaxial type (n = 2), clinodactyly (n=1), curly or overlapping toes (n = 4), and coronal (first degree) hypospadias (n=lO)) were also removed from consideration. All reviews and exclusions were made without prior knowledge of exposure.

The relationship between drugs that were used by at least 200 mothers and defects in their infants was analyzed. Exposure was considered to have occurred during the first month of pregnancy if a mother's prescription had been filled between 365 and 250 days before delivery. Drug use by mothers of children with disorders was tabulated by hand. For the population at large, exposure rates were determined by computer files. Contraceptives, antacids, vitamins and minerals, hormones, and topical preparations were not considered.

Reliability : (2) valid with restrictions. Epidemiology studies can be confounded by variables unrelated to treatment.

27.02.2001 (18)

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I U C L I D

Data Set

Existing Chemical : Butanedioic acid, sulfo-, 1,4-dicyclohexyl ester, sodium salt
CAS No. : 23386-52-9

Printing date : 30.04.2001

1. General Information

Id 23386-52-9
Date 30.04.2001

1.2 SYNONYMS

Succinic acid, sulfo-,1 ,4-dicyclohexyl ester, sodium salt

Dicyclohexyl sodium sulfosuccinate

2.1 MELTING POINT

Value	:	ca. 273 - 350" C
Method	:	other: calculated
Year	:	2000
GLP	:	not applicable for estimations
Test substance	:	succinic acid, sulfo-,l ,4-dicyclohexyl ester, sodium salt
Remark	:	The melting point was estimated using the EPIWIN model based on molecular structure and functionality.
Reliability	:	(2) valid with restrictions. Data were obtained by modeling.

03.03.2001

2.2 BOILING POINT

Value	:	> 300" C at 1 hPa
Decomposition	:	yes
Method	:	other: calculated
Year	:	2000
GLP	:	not applicable for estimations
Test substance	:	succinic acid, sulfo-,l ,4-dicyclohexyl ester, sodium salt
Remark	:	The substance is a salt with negligible volatility. It decomposes on heating above 300 degrees C. The boiling point was estimated using the EPIWIN model.
Reliability	:	(3) invalid. Material will decompose before boiling.

03.03.2001

2.4 VAPOUR PRESSURE

Value		< .00001 hPa at 25" C
Method		other (calculated)
Year		2000
GLP		not applicable for estimations
Test substance		succinic acid, sulfo-,1 ,4-dicyclohexyl ester, sodium salt
Remark		The substance is a salt, and has negligible vapor pressure. The vapor pressure was estimated using the EPIWIN model, based on molecular structure and functionality.
Reliability		(2) valid with restrictions. Data were obtained by modeling.

03.03.2001

2.5 PARTITION COEFFICIENT

Log **Pow**	:	ca. 1.76 at 25" C
Method		other (calculated)
Year	:	2000
GLP	:	not applicable for estimations
Test substance	:	succinic acid, sulfo-,1 ,4-dicyclohexyl ester, sodium salt
Remark	:	The partition coefficient was estimated using the EPIWIN/KOWWIN model based on molecular structure and functionality.

Reliability : (2) valid with restrictions. Data were obtained by modeling.
03.03.2001

2.6.1 **WATER SOLUBILITY**

Value : 12.0g/ 100 ml at 25 °C
Method : no data
Year : 2001
GLP : no data
Test substance : succinic acid, sulfo-,I ,4-dicyclohexyl ester, sodium salt

Remark : Data were supplied by the manufacturer.

Reliability : (2) valid with restrictions. Details on how value was obtained are unknown.
03.03.2001 (4)

3.1.1 PHOTODEGRADATION

Type	: air
Light source	: other
Rel. **intensity**	: based on Intensity of Sunlight
Direct photolysis	
Halflife t1/2	: ca. 5.2 hour(s) at 25" C
Method	: other (calculated)
Year	: 2000
GLP	: not applicable for estimations
Test substance	: succinic acid, sulfo-,l ,4-dicyclohexyl ester, sodium salt
Result	: The rate constant of 24.6 E-12 cm^3/molecule-sec at 25°C was estimated using AOPWIN, that estimates the rate constant for the atmospheric gas-phase reaction between photochemically produced hydroxyl radicals and ozone with organic chemicals. The rate constant estimated by the program was used to calculate the atmospheric half-life based upon the average atmospheric concentration of hydroxyl radicals.
Reliability	: (2) valid with restrictions. Data were obtained by modeling.
03.03.2001	

3.1.2 STABILITY IN WATER

Type	: abiotic
t1/2 pH7	: ca. 14.5 years at 25" C
t1/2 pH 8	: ca. 1.5 years at 25" C
Method	: other (calculated)
Year	: 2000
GLP	: not applicable for estimations
Test substance	: succinic acid, sulfo-,l ,4-dicyclohexyl ester, sodium salt
Remark	: Stability half-lives were estimated using the EPIWIN/HYDROWIN model, based on molecular structure and functionality.
Reliability	: (2) valid with restrictions. Data were obtained by modeling.
03.03.2001	

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	: fugacity model level III
Media	: water - soil
Air (level III)	: .875
Water (level III)	: 40.8
Soil (level III)	: 58.3
Method	: other
Year	: 2000
Test substance	: succinic acid, sulfo-,l ,4-dicyclohexyl ester, sodium salt
Remark	: Level III Fugacity was estimated using the Mackay model (the currently accepted model for estimation of theoretical distribution) with standard defaults. Of the 58.3% shown for soil, 0.1% is estimated to be in sediment and the remainder in soil.
Result	: The Henry's Law constant is estimated by the EPIWIN model to be 3.14E-13, based on molecular structure and functionality. The Koc is estimated by

EPIWIN/PCKOC to be 111. This Koc value indicates moderately low mobility through soil.

Reliability : (2) valid with restrictions. Data were obtained by modeling.
03.03.2001

3.5 **BIODEGRADATION**

Type	: aerobic
Inoculum	: activated sludge
Degradation	: = 35.9% after 28 day
Kinetic of test substance	: 7 day 31.4 % 14 day 39.4 % 21 day 33.7 % 28 day 35.9 %
Control substance	: aniline
Kinetic	: 7 day 84.3 % 28 day 86.7 %
Deg. **Product**	: not measured
Method	: OECD Guide-line 301 E "Ready biodegradability: Modified OECD Screening Test"
Year	: 1988
GLP	: yes
Test substance	: succinic acid, sulfo-,1 ,4-dicyclohexyl ester, sodium salt

Result : There was no significant difference between the results of both tests. Biodegradation (average of 31.4%) occurred within the first seven days of the test and remained relatively constant throughout the study. The test material is not considered "readily" biodegradable according to OECD guidelines. The results of the test were considered valid because aniline was readily biodegraded.

Test condition : The test compound was dissolved in deionized water to make a stock solution of 14%. Test material was diluted to a concentration of 31.5 mg/l with inorganic nutrient medium and the medium was inoculated with micoorganisms from a mixed population. Aniline (30.0 mg/l) was used as a positive control. Test and positive control flasks were shaken for 28 days at 20-25" C in the dark. Tests were performed in duplicate. Biodegradation was followed by dissolved organic carbon (DOC) analysis. Results are reported as the average of the two tests. Results were corrected for blanks without inoculum (except on day 0).

Test substance : Test substance was 53% carbon by analysis.

Reliability : (1) valid without restriction
03.03.2001

(9)

Type	: aerobic
Inoculum	: other:predominantly gram negative bacteria
Concentration	: 1 .25 mmol/l
Contact time	: 4 hour(s)
Result	: other:not readily biodegradable
Method	: other
Year	: 1999
GLP	: no data
Test substance	: other TS

Result : A biodegradation rate of 11.4 micromoles surfactant/min.g cell protein was calculated for di(2-ethylhexyl) sodium sulfosuccinate

Test condition : The bacterial consortium was obtained from a detergent-polluted soil by enrichment cultivation and adaptation in the presence of Surfactant 9 (mono-n-dodecyl sulfosuccinate). Bacteria were cultivated under aeration at 2.5" C in a phosphate mineral medium. Surfactant 9 was added to the culture in a crystalline form to a final concentration of 0.5 g/l. Microscopic examination of microorganisms present in the adapted mixed culture revealed predominantly Gram-negative motile bacteria. The rate constants of primary biodegradation of 10 different alkyl sulfosuccinates (including dicyclohexyl sodium sulfosuccinate) at a concentration of 1.25 mmol/l by the adapted mixed culture (ceil protein 0.4 g/l) was measured at 25" C over 4 hours. The culture was incubated under stirring and samples were taken (times not noted) to determine the amount of surfactant remaining. The extent of biodegradation was estimated as a loss of methylene blue active substances in a chloroform extract of the media. The rate constants were calculated as maximum rates of primary degradation catalyzed by one gram of biomass protein in the initial phase of the reaction.

Test Substance : The test substance was listed as the di-cycle-hexyl ester of sulfosuccinic acid. Other studies performed by the authors list the supplier as Cytec. Cytec markets this material as the sodium salt. Therefore, it is likely that the material used was the sodium salt.

Reliability : (2) valid with restrictions
27.02.2001

(11)

3.7 BIOACCUMULATION

Species : other
BCF : ca. 3.16 at 25" C
Method : other: calculated
Year : 2000
GLP : not applicable for estimations
Test substance : succinic acid, sulfo-,l ,4-dicyclohexyl ester, sodium salt

Remark : The bioconcentration factor was estimated based on molecular structure and functionality using EPIWIN model.

Reliability : (2) valid with restrictions. Data were obtained by modeling.
04.03.2001

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	: static
Species	: Lepomis macrochirus (Fish, fresh water)
Exposure period	: 96 hour(s)
Unit	: mg/l
Analytical monitoring	: no data
NOEC	: m = 240
LC50	: c = 470
Method	: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year	: 1987
GLP	: yes
Test substance	: succinic acid, sulfo-,l ,4-dicyclohexyl ester, sodium salt

Result : Water condition: Dissolved oxygen concentrations ranged from 1 .1 to 8.5 mg/l during the test. They decreased with increasing time of test; dissolved oxygen ranged from 1.1 to 4.0 mg/l (13-48% dissolved oxygen) at 48 and 96 hours. The control chamber remained at above 73% saturation throughout the 96-hour test. At 24 hours, tanks with 1000 mg/l appeared cloudy. After 48 hours and for the remainder of the study, all test tanks were slightly cloudy.

Test Results: None of the controls or fish exposed to 240 or 320 mg/l of test material died. The corresponding mortalities at 48 or 96 hours for fish exposed to 420, 560, 750 and 1000 mg/l were 20%, 90%, 100% and 100% respectively. The majority of these mortalities occurred by 24 hours. Abnormal effects such as surfacing, loss of equilibrium, fish on the bottom of the test chamber, quiescence and/or labored respiration were noted in fish exposed to 320 mg/l or more test compound. The NOEC was 240 mg/l, based on the lack of mortality and abnormal effects.

Test condition : Fish were acclimated for at least 14 days prior to testing. Fish received a standard commercial fish food occasionally supplemented with brine shrimp daily until 48-96 hours prior to testing. Fish were not fed during testing. A 96-hour static bioassay was conducted on IO fish per test group at the following concentrations: 0 (Control), 240, 320, 420, 560, 750, and 1000 mg/l. The average weight and length of the fish were 0.23 g and 22 mm, respectively. Tests were performed in 5-gallon glass vessels containing 15 l of reconstituted water. Water was prepared to yield a total hardness of 40-48 mg/l as $CaCO_3$, a total alkalinity of 25-35 mg/l as $CaCO_3$ and an initial pH of 7.2 to 7.6. Test vessels were maintained at 22 +/- 1.0° C and were not aerated. Fish were observed every 24 hours for abnormal effects and lethality.

The LC_{50} values were calculated by a computer program that utilized data from the binomial, moving average and probit tests.

Reliability : (2) valid with restrictions. Results at the high concentrations may have been confounded by low dissolved oxygen concentration and test material insolubility.

03.03.2001 (3)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	: static
Species	: Daphnia magna (Crustacea)
Exposure period	: 48 hour(s)
Unit	: mg/l

Analytical monitoring	:	**yes**
NOEC	:	m = 90
EC50	:	c = 457
EC100	:	m = 1000
Method	:	OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilisation Test"
Year	:	**1993**
GLP	:	**yes**
Test substance	:	succinic acid, sulfo-,1 ,4-dicyclohexyl ester, sodium salt
Result	:	There was no evidence of insolubility of test material in any of the chambers. Measured concentrations of test material were 80% or greater than nominal concentrations, therefore nominal values were used for the statistical analyses. No immobilization was noted at concentrations lower than 300 mg/l. At 300 mg/l, 15% mobilization was noted at 48 hours. Treatment with 1000 mg/l caused 100% mobilization within 24 hours
Test condition	:	Nominal treatment levels were 8.1, 27, 90, 300 and 1000 mg/l. Individual treatment solutions were prepared by adding the appropriate amount of test material to laboratory dilution water (100 ml) in glass aspirator bottles. Solutions were mixed for approximately 1 hour, after which they appeared clear. The water accommodated fraction (WAF) of each treatment solution was drawn through the outlet at the bottom of the vessels and divided into 4 replicate chambers (25 ml each). Samples were analyzed for test material, dissolved oxygen, temperature and pH. Test chambers were covered with glass to minimize evaporation and/or volatilization. Daphnids were less than 24 hours old when exposure was initiated. Five daphnids were housed in each chamber. The daphnids were exposed to the Water Accommodated Fraction (WAF) of each treatment solution at 20" C in the dark for a 48-hour period. Observations for immobilization, abnormal behavior and appearance were performed at 24 and 48 hours. Water quality measurements (pH, dissolved oxygen and temperature) were performed at study termination. The 48-hour EC50 value was determined using the Spearman-Karber method.
Reliability	:	(I) valid without restriction

03.03.2001 (5)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Selenastrum capricornutum (Algae)
Endpoint	:	growth rate
Exposure period	:	96 hour(s)
Analytical monitoring	:	no data
Method	:	OECD Guide-line 201 "Algae, Growth Inhibition Test"
NOEC	:	none determined
Year	:	1993
GLP	:	**yes**
Test substance	:	succinic acid, sulfo-,1 ,4-dicyclohexyl ester, sodium salt
Result	:	In general, the effect of the test material was stimulatory instead of inhibitory, but no clear dose response trend was present. No EC_{50} value or NOEL could be determined. The growth rate of algae exposed to 8.1 and 90 mg/l was stimulated at 72 (+35.1% and 44.1%, respectively) and 96 hours (+ 64.5% and 57.8%, respectively). Exposure to 300 mg/l stimulated growth by 96 hours (+ 38.2%). Growth at the 90 mg/l treatment was significantly different from the control at 72 (+ 130%) and 96 hours (+ 243%) due to stimulation.
Test condition	:	Treatment solutions (0, 8.1, 27, 90, 300 or 1000 mg/l) were prepared by

adding the appropriate amount of test material to algal nutrient media. Solutions were mixed for approximately 1 hour, after which they appeared clear. The Water Accommodated Fraction (WAF) was drawn through an outlet at the bottom or the vessels and analyzed analytically for test material. The pH of each treatment was measured and adjusted to 7.5 +/- 0.1, as necessary. A 50 ml aliquot of each solution was removed to serve as a blank.

Each treatment solution (150 mL) was inoculated with Algae (S. capricornutum; 7500 to 9100 cells/ml) and divided into 3 replicate chambers (50 ml/125 ml flask). Test chambers were closed with cotton-gauze stoppers during the study to minimize evaporation and/or volatilization. Test flasks were shaken (100 rpm) to keep algae in suspension and facilitate transfer of CO_2. Algae were incubated for 96 hours at 23.2 +/- 0.2" C under continuous light.

Cell densities were determined for each replicate chamber at 1, 24, 48, 72 and 96 hours. The pH was measured at Day 0 and at termination.

Data were evaluated using the ANOVA procedure of SAS for NOEC determination. An inverse interpolation method was used for the EC_{50} determination.

Reliability : (1) valid without restriction
03.03.2001 (6)

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

Species	: Other:Tradescantia bicolor
Endpdoint	: necrosis
Exposure period	: 48 hour(s)
Unit	: mmo/l
NOEC	: m = 1.25
Method	: other
Year	: 1999
GLP	: no data
Test substance	: other TS

Result : At 24 hours, the necrosis scores for all test concentrations except 20 mmol/l were 0. The score for 20 mmol/l was 1. At 48 hours, concentrations of 1.25 mmol/l and lower had no effect. A concentration of 2.5 mmol/ induced a score of 1. Higher concentrations produced scores of 2.

Test condition : Eleven different sulfosuccinate esters were tested. Solutions of the di-cycle-hexyl ester of sulfosuccinic acid were tested at 0.3125, 0.625, 1.25, 2.5, 5, 10 and 20 mmolll. Test solutions were infiltrated into leaf sheets of Tradescantia bicolor plants (approximately an area of IO x IO mm). Distilled water was used as a control. Each experiment was run in triplicate. Phytotoxicity was evaluated after 24- and 48- hours and was scored according to the following method (0 = no effect, 1 = no necrosis but infiltrated area appears yellow, 2 = necrosis). A spectral mapping technique was used to analyze the effects of the ester compared to the other esters tested.

Test substance : The test substance was listed as the di-cycle-hexyl ester of sulfosuccinic acid. Other studies performed by the authors list the supplier as Cytec. Cytec markets this material as the sodium salt. Therefore, it is likely that the material used was the sodium salt.

Reliability : (1) valid without restriction
03.03.2001 (8)

5.1.1 ACUTE ORAL TOXICITY

Type	: LD50
Species	: rat
Strain	: Wistar
Sex	: male
Number of animals	: 20
Value	: = 3540 mg/kg bw
Method	: other
Year	: 1969
GLP	: pre-GLP
Test substance	: other TS

Result : Signs of intoxication included diarrhea, lethargy, prostration, and coma. None of the animals given 1.25 or 2.5 g/kg died or appeared intoxicated, All animals in the 5.0 and 10.0 g/kg groups died.

Test condition : Twenty male rats (average weight 150-265 g) were fasted for 24 hours before dosing. Animals (5 per group) were dosed with a 20% w/v aqueous dispersion of the product at 1.25, 2.5, 5.0 or 10.0 g/kg. Animals were observed for behavior and death over a 6-hour period.

Test substance : Material tested was 80% CAS # 23386-52-9, 12% H_2O, and 8% ethanol

Reliability : (1) valid without restriction
03.03.2001 (1, 10)

51.3 ACUTE DERMAL TOXICITY

Type	: LD50
Species	: rabbit
Strain	: other:albino
Sex	: male
Number of animals	: 10
Value	: > 5000 mg/kg bw
Method	: other
Year	: 1969
GLP	: pre-GLP
Test substance	: other TS

Result : One out of the 10 animals died. Signs of intoxication included hind leg weakness, skin irritation, severe erythema and severe edema followed by eschar formation. Gross autopsies of all survivors appeared normal. The LD_{LO} was 5 g/kg.

Test condition : An aqueous paste of the product was held under an impervious cuff in continuous 24-hour contact with the shaved skin of 10 male albino rabbits (mean wt 2.84 kg) at a dosage of 5.0 g/kg. Animals were observed for up to 14 days.

Test substance : Material tested was 80% CAS # 23386-52-9, 12% H_2O, and 8% ethanol

Reliability : (1) valid without restriction
03.03.2001 (1,10)

5.4 REPEATED DOSE TOXICITY

Species : rat

Sex	: male/female
Strain	: Wistar
Route of admin.	: oral feed
Exposure period	: 32 days
Doses	: 0.25, 0.5 and 1 .0%
Control group	: **yes**
NOAEL	: > 1 **%**
Method	: other
Year	: 1969
GLP	: pre-GLP
Test substance	: other TS

Result : There were no deaths and the overall appearance and behavior of both the test and control animals were good. No relevant gross lesions were observed in treated animals. There were no significant differences in mean food intake, mean weight gain, or mean adjusted weight gain between the test and control groups.

Test condition : The product was incorporated into the diet to give concentrations of 0.25, 0.5, and 1 .0% (mean dose 240, 470 and 960 mg/kg/day). Diets were fed to young rats (5/sex/group) weighing an average of 143 g for 32 days. A control group of 10 rats/sex was included. Behavior, food intake and weight were monitored over the course of the study. Animals were terminated 32 days after study initiation, and autopsies were performed on high-dose animals. Since there was no sex-related effect of treatment, results from males and females were combined for statistical analyses. The method of multiple comparisons was used to evaluate food intake and weight gain data.

Test substance : Material tested was 80% CAS # 23386-52-9, 12% H_2O, and 8% ethanol

Reliability : (1) valid without restriction
03.03.2001 (1)

Species	: rat
Sex	: male/female
Strain	: other:Charles River albino
Route of admin.	: oral feed
Exposure period	: 90 days
Doses	: 1.0%
Control group	: **yes**
NOAEL	: > 1 %
Method	: other
Year	: 1969
GLP	: pre-GLP
Test substance	: other TS

Result : No deaths or abnormal behavioral reactions were noted in treated animals. There was no effect of treatment on final body weight, food consumption, hematologies, urinalyses, or gross or histopathology (as compared to controls).

Test condition : Design: 20 albino rats / sex were fed test material for 90 days at a dietary concentration of 1 .0%, which **was** prepared by blending the appropriate amount of test material with standard rat ration. Twenty control rats/sex received normal food. Rats were weighed biweekly and food consumption was recorded weekly. Fresh diets were prepared weekly. Standard hematologies and urinalyses were performed on blood and urine samples collected from 5 rats/sex/group on treatment day 84.

Endpoints: Animals were sacrificed 90 days after treatment and a complete

set of organs and other tissues were examined. At autopsy, the weight of the liver and kidneys of 10 rats/sex/group were recorded. The following tissues from 5 rats/sex/group were examined histologically:esophagus, stomach (cardia, fundus, pyloris), small intestine (duodenum, jejunum, ileum), cecum, colon , liver, kidneys, spleen, pancreas, urinary bladder, pituitary, adrenal, testes, seminal vesicle, ovary, bone marrow, thyroid, parathyroid, salivary gland, prostate, heart, aorta, lung, lymph node (cervical and mesenteric), skeletal muscle, peripheral nerve, bone (femur), spinal cord, uterus, trachea, eye, optic nerve and brain (cerebrum, cerebellum, and pons).

Statistical Analyses: Data for food consumption, weight, absolute organ weights and organ/body weight ratios were analyzed by analysis of variance (ANOVA). Effects uncovered were further analyzed by t-tests.

Test substance : A commercial sample of the material was dried to remove the liquid phase. The dried products were 100% solids or "active ingredients"

Reliability : (1) valid without restriction
02.03.2001 (7)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test
Concentration : 1 mg/plate
Metabolic activation : without
Result : negative
Method : other
Year : 1976
GLP : pre-GLP
Test substance : succinic acid, sulfo-,1 ,4-dicyclohexyl ester, sodium salt

Test condition : Salmonella typhimurium strains TA-98, TA-100, TA-1535, WP-2 uvrA-, TA-1530 and TA 1538 (1 x 1 OE8) were plated with 1000 micrograms test material per disc or plate according to the method of Ames. Plates were not supplemented with S9. There were no positive controls.

Reliability : (2) valid with restrictions. Methodology was poorly documented. There were no positive controls.
03.03.2001 (2)

5.8 TOXICITY TO REPRODUCTION

Type : other:histopathology of reproductive organs
Species : rat
Sex : male/female
Strain : other:Charles River albino
Route of admin. : oral feed
Exposure period : 90 days
Doses : 1.0%
Method : other
Year : 1969
GLP : pre-GLP
Test substance : other TS

Remark : This study was part of a 90-day oral toxicity study described in Section 5.4

Result	:	There was no effect of treatment on any reproductive organ
Test condition	:	Twenty albino rats I sex were fed test material for 90 days at a dietary concentration of 1 .0%, which was prepared by blending the appropriate amount of test material with standard rat ration. Animals were sacrificed after 90 days of treatment and were subjected to gross pathology. Ovaries and uteri from females and prostate, testes and seminal vesicles from males were examined histologically.
Test substance	:	A commercial sample of the material was dried to remove the liquid phase. The dried products were 100% solids or "active ingredients"
Reliability 03.03.2001	:	(1) valid without restriction (7)

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